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THE DIAGNOSIS OF DISLOCATION OF THE HIP IN NEWBORNS AND THE PRIMARY RESULTS OF IMMEDIATE TREATMENT

by

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In 1935 ORTOLANI described a simple method for detecting congenital dislocation of the hip in newborns, by forced abduction which causes a 'click' as the head snaps over the socket wall. Though this method appears to be reliable, roentgen examination is desirable not only to confirm the diagnosis but also to evaluate the immediate results of treatment.

Various roentgen methods have been suggested for demonstrating congenital dislocation of the hip in newborns (HILGENREINER, OMBREDANNE, SHANTON-MENARD, and others).

Since the femoral head and neck and the greater trochanter are not ossified at birth and since the acetabulum then consists mainly of cartilage, the position of the head in relation to the acetabulum can only be demonstrated indirectly.

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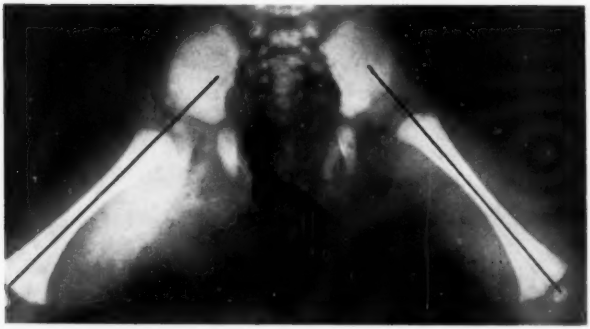

Fig. 1. Roentgenograms (post mortem) of newborn with femur abducted and rotated inwards. *Right side:* Normal hip, femoral shaft directed towards edge of acetabular wall. *Left side:* Dislocation, femoral shaft directed towards anterior superior iliac spine. (Ortolani's "click" could be elicited on this side but not on the right).

All the roentgen methods available are based on measurements of various distances and angles in a. p. roentgenograms of the pelvis with the legs extended. However, owing to the latitude in the normal measurements, it is sometimes difficult, if not impossible, to decide with certainty whether a hip in a given case should be regarded as dislocated or not. CAFFEY et coll. (1956), for example, claimed on the basis of 627 examinations that 'there is no support in our findings, by far the most comprehensive to date, for a congenital dysplasia-predislocation hypothesis of congenital dislocation of the hip based on an enlarged acetabular angle...'

The authors have worked out a simple roentgen method for demonstrating congenital dislocation of the hip in newborns on the basis of certain theoretical considerations. It was considered that in the elaboration of a reliable method for demonstrating congenital dislocation of the hip the following principles should be followed:

1. The femora should be kept dislocated during the exposure of the film.

2. The diagnosis should not depend on the size of the angles between lines drawn from ill-defined points, *e. g.* the acetabular angle.

3. The diagnosis should not be based on uncertain measurements such as the one involving the upper end of the femoral diaphysis; these may vary widely from one infant to another (ZSEBÖK).

4. The result should preferably be conclusive and leave no room for doubt, *i. e.* it should be possible to decide with certainty whether a hip is dislocated or not.

Fig. 2. Same case as in fig. 1. Arthrographic appearance of dislocated hip.

Method

It appears that the above-mentioned requirements can be fulfilled by forcible abduction — to at least 45° — with appreciable inward rotation of the femora (Fig. 1). This manipulation displaces the head medially with the result that it is forced either into or out of the socket depending on the presence or absence of dislocation, so that the head never assumes an intermediate position. If the hip is normal, the line of the femoral shaft will be directed towards the upper edge of the bony acetabular wall, but in the presence of congenital dislocation of the hip, it will point to the anterior superior iliac spine. Both reference points as well as the direction of the longitudinal axis of the femoral shaft are readily defined. It should be stressed that abduction should be about 45° or more, otherwise the roentgenograms may be misleading (Fig. 3) and further that owing to the marked antetorsion of the femoral neck in newborns, a fair degree of inward rotation of the femora is necessary. If the dislocation is considerable with much upward displacement of the femur, it may be difficult to secure rotation of the femur, but even then the shaft should lie directed towards the iliac spine (Fig. 4, upper view).

Only if the hip is actually dislocated at birth can a roentgen examination of a newborn be expected to yield reliable information. According to general consensus, the dislocation is as a rule not congenital but secondary to congenital hypoplasia. Our material, however, provides no support for this opinion.

During the last 5 years 99.5 per cent (15,373) of all children in Malmö were born in this hospital and were examined by ORTOLANI's method by pediatricians.

Fourteen cases of congenital dislocation of the hip were discovered. The dislocations were bilateral in 13 and unilateral in one case. Only one of the children was a boy. In addition one left-sided dislocation was detected post mortem in a boy who had died a few hours after birth (Figs. 1 and 2). The frequency was thus 0.1 per cent, which more or less agrees with the

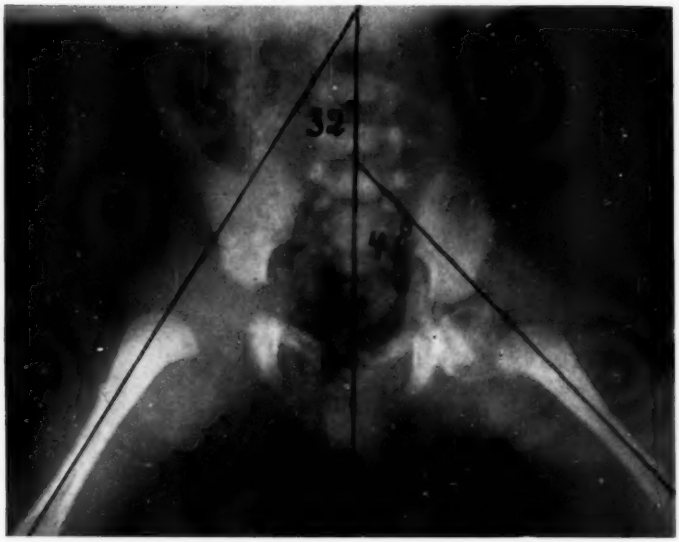

Fig. 3. Post-mortem roentgenogram (arthrogram on left side) showing that abduction appreciably less than 45° can give misleading results. Normal case.

overall frequency of 0.09 per cent given by SEVERIN (1956) for verified dislocation of the hip in Sweden. Since the General Hospital is the only one catering for the population (more than 200,000 inhabitants) of Malmö, any cases of dislocation detected later in infancy would have been brought to our notice, but during the last 5 years no such cases have been reported or seen. This then strongly suggests that both 'overdiagnosis' and 'underdiagnosis' can be ruled out and that the dislocation really is congenital. Adequate treatment of cases detected at birth was not followed by any roentgenologically demonstrable hypoplasia. This together with the fact that underdiagnosis can evidently be excluded strongly suggests that 'dysplasia' is a result and not a cause of congenital dislocation of the hip.

In our material, treatment of the last 8 cases consisted of placing the child in an aluminium splint to hold the legs abducted and rotated outwards, *i. e.* in a position of reduction (Fig. 4, lower view). If treatment is started immediately after birth, immobilisation of the hip in this position for a few weeks is probably sufficient. Fig. 5 shows the same hips as Fig. 4, but after 16 days' immobilisation in an aluminium splint; the joint could then no longer be dislocated.

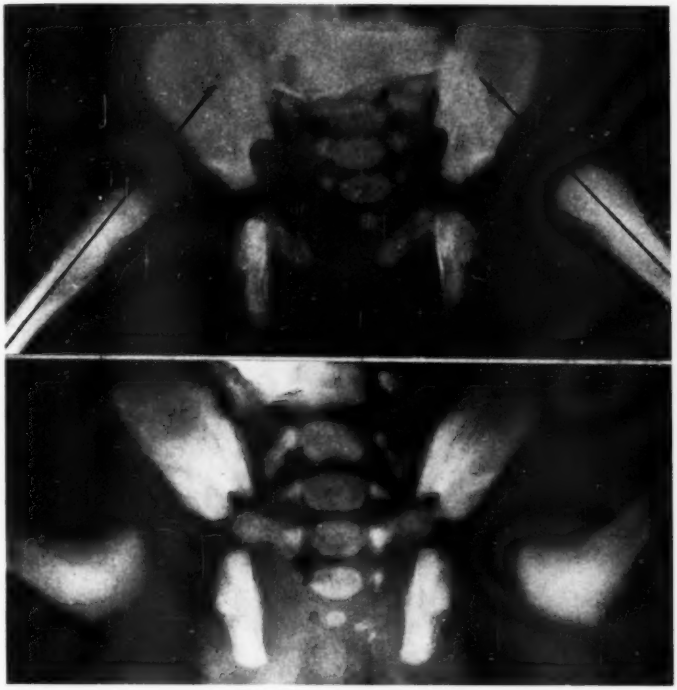

Fig. 4. Bilateral dislocations. *Upper* view: Shafts directed approximately towards superior anterior iliac spines despite limited inward rotation of femora. *Lower* view: Roentgenogram of hips in reduced positions on same occasion.

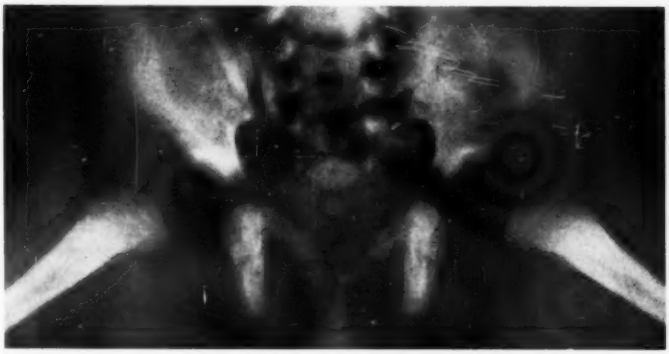

Fig. 5. Same case as in fig. 4, after 16 days' treatment. Dislocation no longer possible.

Conclusions

The observations presented suggest the following conclusions:

1. ORTOLANI's simple method for demonstrating the dislocation of the hip in newborns is reliable.

2. Dislocation of the hip is congenital and appears to be the cause and not the result of hypoplasia.

3. If treatment is started immediately, a few weeks' immobilisation of the hip is probably sufficient.

4. With the roentgen method described, it is possible to demonstrate a dislocation of the hip in newborns with certainty and also to evaluate the immediate results of treatment.

SUMMARY

A roentgen method is described for diagnosing dislocation of the hip in newborns, the material consisting of 15,373 cases in 14 of which congenital dislocation of the hip was found (0.1 %). Observations made in the present investigations strongly suggest that dislocation of the hip in newborns is actually congenital and that hypoplasia is a result rather than the cause of the condition. The treatment is mentioned.

ZUSAMMENFASSUNG

Eine Röntgenmethode zur Diagnostizierung von Dislokationen in den Hüftgelenken von Neugeborenen wird beschrieben. Das Material besteht aus 15,373 Fällen; in 14 von diesen wurde Hüftgelenksdislokation gefunden (0.1 %). Die in der vorliegenden Untersuchung gemachten Beobachtungen betonen stark, dass die Hüftgelenksdislokation bei Neugeborenen wirklich kongenital ist und dass die Hypoplasie eher die Folge als die Ursache dieses Zustandes ist. Die Behandlung wird erwähnt.

RÉSUMÉ

Les auteurs décrivent une méthode radiologique pour le diagnostic de la luxation de la hanche chez les nouveau-nés; ils ont étudié 15,373 cas sur lesquels ils ont trouvé 14 cas de luxation congénitale de la hanche (9.1 %). Les observations faites au cours de ces recherches incitent nettement à penser que la luxation de la hanche chez les nouveau-nés est réellement congénitale et que l'hypoplasie est une conséquence plutôt que la cause de cette affection. Le traitement est envisagé.

REFERENCES

CAFFEY, J., AMES, R., SILVERMAN, W., RYDER, C. T. and HOUGH, G.: Congenital dislocation of the hip. Pediatrics 17 (1956), 632.

GLAUNER, R. und MARQUARDT, W.: Röntgendiagnostik des Hüftgelenks. Georg Thieme Verlag, Stuttgart 1956.

ORTOLANI, M.: La Lussazione congenita dell'anca. Cappelli Editore, Bologna 1948.

VON ROSEN, S.: Early diagnosis and treatment of congenital dislocation of the hip joint. Acta Orthop. scand. 26 (1956), 136.

SEVERIN, E.: Frekvensen av luxatio coxae congenita och pes equino-varus congenitus i Sverige. (In Swedish.) Nord. Med. 55 (1956), 221.

ZSEBÖK, Z.: Röntgenanatomische Untersuchungen am Beckengürtel des Neugeborenen. Fortschr. Röntgenstr. 87 (1957), 23.

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DOUBLE-CONTRAST ROENTGENOGRAPHY OF THE STOMACH

A study on the applicability of direct air insufflation in gastric diagnosis

by

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The techniques employed in the roentgen examination of the stomach still appear to leave a great deal to be desired. While organic changes on the lesser curvature, or in the duodenal bulb are readily demonstrated, it may be difficult to diagnose changes on the anterior and posterior gastric walls even if relief studies and compression techniques are used. However, certain regions have always presented particular difficulties, viz. the cardia, fornix, and the upper part of the body, since because of their location behind the costal arch they are inaccessible to direct palpation.

The desire for improved diagnostic methods in these parts of the stomach has led to the development of various forms of double-contrast examinations.

By double-contrast roentgenography of the stomach must be understood any method in which a roentgen opaque substance, usually barium

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sulphate, is used together with a transparent medium. Rice flour porridge (BAASTRUP 1924, 1926), mineral oil (GIANTURCO 1949), and gas have been used as the transparent component. The first two have not been used very much. The combination of barium sulphate and gas has been employed for a long time, principally by the administration of effervescent powders (VALLEBONA 1931, FEISSLY 1930, and others). Even though this method has been widely used, its shortcomings are conspicuous. First, it is necessary to give a little water with the powders, this often having the effect of washing the opaque medium away from the gastric wall. Secondly, gas bubbles may be formed in the medium, and tend to counteract the demonstration of finer detail. Further drawbacks are the difficulty in controlling the amount of distension of the stomach and the spoiling of the examination by eructations of wind. Even though this method is rapid and easy to perform, its diagnostic applicability is in the author's opinion fairly limited. Closely related to this technique is the administration of soda water (BENDICK 1951, 1954). As shown by the illustrations in BENDICK's paper of 1954, this technique may yield excellent results in the hands of an experienced radiologist.

In order to obtain better demonstration of the gastric wall, air has been introduced into the stomach through a thin rubber tube following the administration of the contrast medium. Two different methods are used: one employs air insufflation into a thin-walled rubber balloon; in the other air is introduced directly into the stomach.

The introduction of a balloon into the stomach, which was originally used by physiologists, with or without the simultaneous use of an opaque medium, for the determination of the intragastric pressure and physiologic gastric motility, was modified for diagnostic purposes by D'ELOIA in 1941. An investigation in which this method was employed was published by LE CANUET et coll. in 1946. It was, however, PIRKEY et coll. (1949, 1952) who seem to have taken advantage of the possibilities of the method.

Insufflation of the stomach through a thin rubber tube, without the use of a balloon, was described by HILPERT in 1928. Both HILPERT, and later COLCHER (1937), attached importance to the preservation of the gastric mucosal folds by introducing only small quantities of air in an attempt to further the study of the mucosal relief, while WASCH and EPSTEIN (1944) and RUZICKA and RIGLER (1951) aimed at a high degree of distension of the stomach. ALBOT et coll. (1946), who directed their studies chiefly to the fornix, used a similar technique.

Neither the balloon method nor direct air insufflation, in combination with the administration of an opaque medium, seems to have received much attention in the Scandinavian literature, although BAASTRUP (1924) published some experimental studies and LYSHOLM (1937) pointed out the value of gastric insufflation especially in cases of suspected tumour, but without the use of an opaque substance.

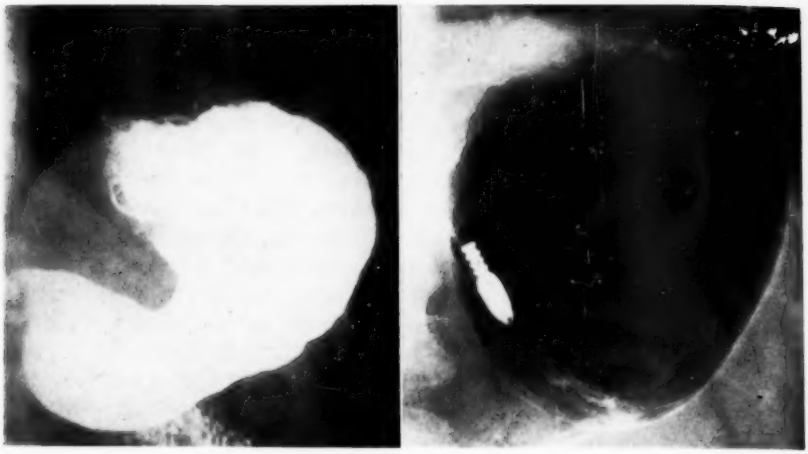

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Fig. 1. a) Ordinary roentgen examination, irregular medial part of fornix. b) Double-contrast examination. Pathologic process in the fornix due to growth. (Reticulosarcoma ventriculi.)

Author's material

Technique. The balloon method, which was used in a small number of cases, will not be considered in detail. Although the number of examinations carried out by this technique is too small to allow of definite conclusions, it is our impression that equally good, if not better results can be obtained by direct air insufflation. This particularly applies if pathologic conditions in the immediate vicinity of the cardia are suspected, since a collection of contrast medium between the balloon and the cardia may render the interpretation of this region difficult. Since direct insufflation is also simpler and causes less discomfort to the patient, this method was preferred.

The method of direct air insufflation of the stomach used in this investigation scarcely differs in principle from the one used by WASCH and EPSTEIN, and RUZICKA and RIGLER. A thin rubber tube is introduced through the nose into the stomach, until the tip lies at the fornix. If the preceding routine examination has revealed hypersecretion or the presence of gas in the stomach, effective aspiration is important. The patient is then given about 15 to 30 ml colloidal barium sulphate (Collo-Bar — UCLAF, Paris), placed in the supine position for a few minutes, turned into the left lateral posture and, finally, in the prone position, in order to

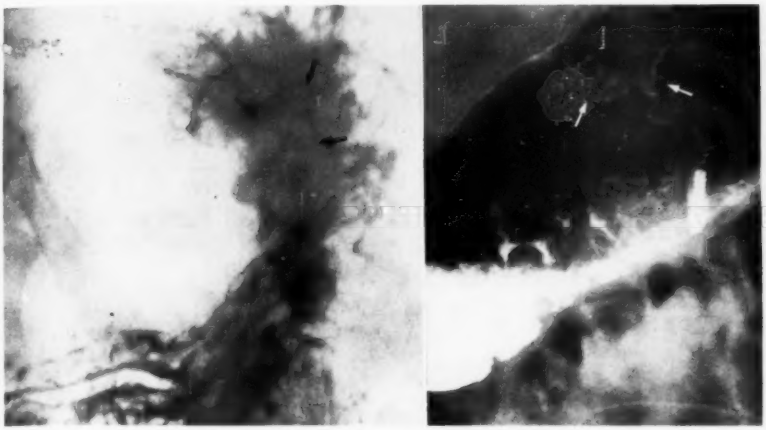

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Fig. 2. a) Ordinary examination. b) Double-contrast examination. Pathologic process, presumably a tumour, on lesser curvature of the stomach. (Carcinoma ventriculi).

obtain the best possible distribution of the contrast medium in the entire stomach.

The introduction of air is performed by means of an ordinary rubber insufflator and continued until fluoroscopic control reveals that a suitable degree of distension of the stomach has been obtained. It may sometimes be necessary to pump in a little more air during the examination if some should escape by eructation or passage into the duodenum.

The amount of air to be introduced depends to some extent on the changes which are suspected. Sparse insufflation (100 to 300 ml air) will to some extent preserve the mucosal folds, which may be useful, especially in the search for gastric ulcers. However, the principle of the method is to smooth out the normal gastric rugae by the insufflation, so that pathologic changes represented by rigid areas may be distinguished. For this purpose, amounts of air ranging from 1,200 to 1,600 ml are introduced; the exact quantity has, however, been measured only in exceptional cases.

If the stomach is empty before the examination, or careful aspiration has been performed, a thin layer of contrast medium will adhere to the gastric wall after the insufflation. In order to obtain a fairly even distribution it is necessary that the medium administered be of suitable consistency. In our series the barium emulsion was of a relatively high viscosity, similar to that used in relief studies; too thick a contrast medium results in a patchy distribution whereas the medium, if too thin, does not adhere properly.

It may be stated as a generalization that the best demonstration of the fornix and the body of the stomach is obtained with the patient in the upright position, and of the antrum with the patient supine. Minor changes cannot be distinguished by fluoroscopy alone, and it is necessary to take films not only postero-anteriorly, but also in both oblique projections. The examination should normally include a lateral view; films taken with the patient prone will rarely be necessary. On the conclusion of the examination the air is allowed to escape through the stomach tube before this is removed.

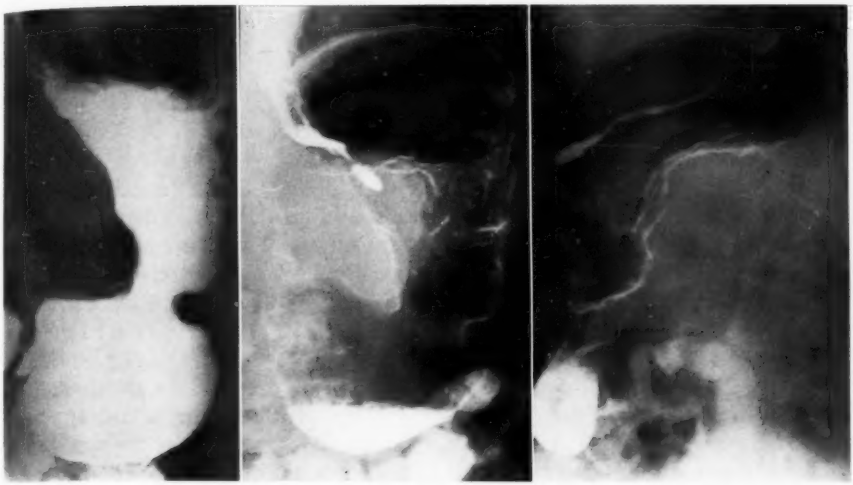
Correct exposure and processing of the film material to ensure suitable contrast is important for showing detail on the anterior and posterior walls of the stomach and of soft-tissue masses protruding into the stomach. This will entail overexposure of the films by increasing the voltage (if necessary, under photometric control) and shortening the developing time.

The examination is not unpleasant to the patient who may previously have experienced the passage of a stomach tube; the air insufflation gives rise only to a sensation of fulness.

It has always been possible to accomplish the examination, even in a few cases of stenosing tumours at the cardia. In such cases, the stomach tube was inserted until distinct resistance was experienced; a little air or barium was then injected through the tube while slight downward pressure was exerted; the procedure was repeated if necessary until the tube entered the stomach.

Case material. The experience so far gained with this technique is based on 95 double-contrast examinations in 92 cases. Operative or autopsy findings have been compared with the radiologic observations in 26 and 7 cases, respectively. Patients who were not subjected to subsequent operation were summoned for one or more control roentgen examinations if the first examination left any doubt as to the correct diagnosis. Controls were carried out in 14 cases from 5 weeks to 8 months (average 20 weeks) after the first examination. Three cases were subjected to gastroscopic examination, which showed fairly good agreement with the radiologic observations.

With the exception of six cases in which the double-contrast investigation was performed in direct connexion with the routine examination of the stomach, and in which both methods showed normal conditions, the former type of investigation was considered to be indicated in cases in which organic gastric changes were suspected. No attempt was made to examine the duodenal bulb even though HAMPTON (1937), MEYER (1952) and HINKEL and MOLLER (1956) obtained satisfactory results in double-contrast studies of this region.



a b c

Fig. 3. a) P.a., erect. Ordinary roentgen examination. b) and c) P.a. and lateral views, erect. Double-contrast examination. Large impression in medial and posterior portions of body with displacement of stomach. No demonstrable intrinsic lesion. (Carcinoma of pancreas.)

Results

The series comprises 22 cases of gastric tumours. Of these, 12 were confirmed by operation and 6 by autopsy. Two of the cases were only subjected to gastroscopic examination, which revealed evidence in support of the radiologic diagnosis, but as the cases were regarded as inoperable, final confirmation was not available.

One of the patients died at home with signs of oesophageal cancer about 6 months after the double-contrast examination had revealed a tumour of the cardia involving the oesophagus and lesser curvature.

A presumably malignant process involving the antrum was revealed in another case, of which there is no after-history.

Good agreement existed in all cases in which it was possible to compare the radiologic observations with operative or autopsy findings. Apart from 1 case in which the tumour was quite definite in both forms of examination, the double-contrast studies gave much more accurate information than the ordinary roentgen examination as to the location and extent of the pathologic changes. In 4 cases, the routine examination failed to reveal any trace of the pathologic process, but the clinical symptoms prompted us to perform a double-contrast investigation.

No fewer than 10 of the tumours demonstrated involved the cardia, fornix, or upper part of the body of the stomach, in agreement with the peculiar diagnostic difficulties experienced in these regions.

It is by no means a rare occurrence that gastric impressions produced by neighbouring organs, especially the splenic flexure of the colon, may lead to diagnostic difficulties. Many of the double-contrast studies were performed because of minor irregularities in the gastric contour; in most cases, it would presumably have been possible to eliminate the possibility of pathologic changes by further examination by the ordinary methods. In 13 cases, the presence of a tumour was strongly suspected at the routine examination, viz. 6 with changes in the cardia and fornix, 4 with changes along the greater curvature, 2 with changes in the antrum, and 1 in which changes along both the greater and lesser curvatures were suspected. In all these cases the double-contrast investigations revealed a normal stomach; in the last-mentioned case an extragastric tumour was diagnosed, and subsequent operation disclosed a pancreatic tumour. In the remaining cases the irregularities were due to physiologic impressions produced by neighbouring organs, sometimes apparently in association with hypertrophic gastritic changes.

The diagnoses were confirmed in six of these cases. Operation revealed carcinoma of the pancreas (the case mentioned above), duodenal bulb ulceration and appendicitis, respectively, in 3 cases, whereas no demonstrable changes of the stomach were present; 1 patient died and was found at autopsy to have had carcinoma of the rectum and a normal stomach. Two patients returned for control roentgen examination 6 and 29 weeks later, at which the stomach showed normal conditions.

In a few cases, the double-contrast examination revealed previously undiagnosed ulceration on the anterior or posterior wall of the stomach. As most gastric ulcers are situated on the lesser curvature and are usually well demonstrated by ordinary roentgenographic methods, double-contrast examinations will scarcely prove to be of any great assistance in the diagnosis of such lesions.

In three cases, a small hiatus hernia which had not been demonstrated by routine roentgen examination was revealed, but the experience gained is too limited to allow of any evaluation of the effectiveness of the method in this field.

Conclusions

As the double-contrast investigation, if it is to include the entire stomach, is more time-consuming than an ordinary examination, and as a report upon the duodenum is always required, the special examination is advocated only as a supplementary procedure to the routine barium meal. This latter is generally adequate in most cases of neoplasm and offers equally satisfactory information in cases of hiatus hernia or gastric ulcer.

In some cases in which the ordinary barium meal leaves some doubt — cases with doubtful filling defects or impressions possibly due to extragastric or intragastric lesions including multiple and solitary polyps — a supplementary examination by the double-contrast method will often be of decisive importance. In the presence of gastric tumours, especially when they involve the cardia or fornix, it is often easier to determine their extent with the double-contrast method.

SUMMARY

Double-contrast examination of the stomach with direct air insufflation following the administration of barium emulsion has been used in a material of 95 cases. The method has proved to be cf value as a supplement to the ordinary examination of the stomach.

ZUSAMMENFASSUNG

Doppelkontrastuntersuchung des Ventrikels mit direkter Luftinsufflation im Anschluss an die Verabreichung von Bariumlösung ist in einem Material von 95 Fällen benutzt worden. Es hat sich ergeben, dass die Methode als Supplement zur üblichen Ventrikeluntersuchung wertvoll ist.

RÉSUMÉ

L'auteur a utilisé sur une série de 95 cas l'examen en double contraste de l'estomac par insufflation directe d'air après l'ingestion du repas baryté. Cette méthode s'est montrée utile comme complément de l'examen habituel de l'estomac.

REFERENCES

Albot, G., Le Canuet, R. et Berthet, G.: Le transit oesophagien avec insufflation gastrique, méthode d'étude des lésions cardiotubérositaires. Arch. mal. app. digestif 35 (1946), 538.

Baastrup, Chr. I.: Roentgenological studies of the inner surface of the stomach and of the movements of the gastric contents. Acta radiol. 3 (1924), 180.

— Some roentgen pictures of the inner surface of the stomach under pathological conditions. Acta radiol. 6 (1926), 122.

Bendick, A. J.: Mucosal aerographic studies of the stomach and small bowel. J. Mt. Sinai Hosp. 17 (1951), 917.

— Diagnostic advances in gastrointestinal roentgenology. Grune & Stratton, New York 1954.

Colcher, M. D.: New displacement technic for study of gastric mucosal relief. Radiology 29 (1937), 615.

D'Eloia, A. S.: Pneumogastroscopy. A preliminary report. Am. J. Surg. 53 (1941), 280.

Feissly, R.: Le poudrage baryté combiné à l'insufflation, pour la mise en évidence, par voie radiographique, du relief de la muqueuse gastrique. Arch. mal. app. digestif 20 (1930), 76.

GIANTURCO, C.: A new method of examination of the gastric mucosa. Am. J. Roentgenol. 62 (1949), 564.

HAMPTON, A. O.: Safe method for roentgen demonstration of bleeding duodenal ulcers. Am. J. Roentgenol. 38 (1937), 565.

HILPERT, F.: Das Pneumo-Relief des Magens. Fortschr. Röntgenstr. 38 (1928), 80.

HINKEL, C. L. and MOLLER, G. A.: Routine barium-gas examination of the duodenal bulb. Am. J. Roentgenol. 75 (1956), 291.

LE CANUET, R., LAPIPE, M. et PICHARD, R.: Une technique d'exploration radiologique de l'estomac. La compression par ballon intragastrique. Arch. mal. app. digestif 35 (1946), 460.

LYSHOLM, ERIK: Gasfilling of the stomach and duodenum as aid in their examination. Acta radiol. 18 (1937), 259.

MEYER, R.: Air-contrast study of duodenal ulcer. Radiology 58 (1952), 393.

PIRKEY, E. L.: Double contrast roentgenograms of the stomach; an additional aid in diagnosis. Am. J. Roentgenol. 62 (1949), 70.

— KERMAN, H. D., REED, E. S., SMITH, W. H. and WHITEMAN, G.: Clinical studies on the use of controlled intragastric pressure for the roentgen diagnosis of lesions in and about the fundus of the stomach. Am. J. Roentgenol. 67 (1952), 217.

— REED, E. S., SMITH, W. H. and WHITEMAN, G.: "Profile line" in roentgenologic differentiation of intrinsic and extrinsic lesions of the stomach. J. A. M. A. 148 (1952), 1095.

RUZICKA, F. F. and RIGLER, L. G.: Inflation of the stomach with double contrast. J. A. M. A. 145 (1951), 696.

VALLEBONA, A. A.: A new combined method of iconography. Reports and communications of the third Intern. Congr. Radiology, p. 309. Masson, Paris 1931.

WASCH, M. G. and EPSTEIN, B. S.: The roentgen visualization of tumors of the cardia. Am. J. Roentgenol. 51 (1944), 564.

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LATE RESULTS OF BRONCHOGRAPHY USING DIONOSIL OILY

by

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The possibility of delayed irritative effects of contrast medium persisting in the lungs following bronchography is well known. With iodised oil, FISCHER (1953) recorded that oil retention for more than 90 days in man is regularly followed by granuloma formation in the lungs. Following the introduction of water-soluble contrast media, granuloma formation was again noted in rats and man and attributed to the presence of carboxy-methyl cellulose (WERTHEMANN and VISCHER 1951). More recently the effects of Dionosil Oily (Glaxo), which is a suspension of propyliodone in arachis oil, have been studied in animal experiments by BJÖRK and LODIN (1957). Using this medium in rabbits they noted the presence of foreign body granulomata in the lungs after bronchography, and this they attribute to the arachis oil. The purpose of this paper is to record the results of bronchography after 5 years continuous use of Dionosil Oily, and to present the histological findings in resected lung tissue previously submitted to this examination.

Method and materials

Bronchography is carried out in these hospitals by two methods. Children under the age of 12 years are usually examined under general

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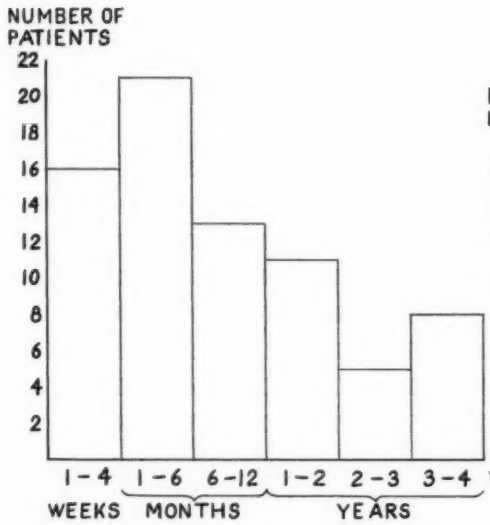

Diagram 1. Time interval between bronchography and operation.

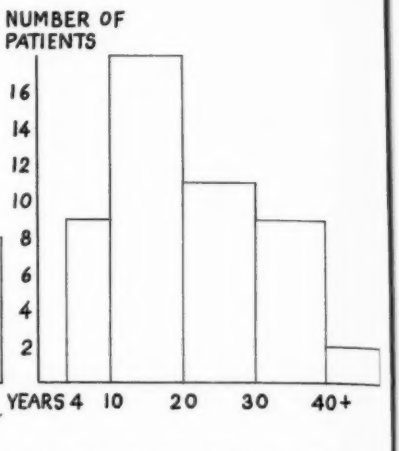

Diagram 2. Age distribution in number of patients examined.

anaesthetic. Pentothal Sodium, with the addition of a muscle relaxant such as Flaxedil (May & Baker Ltd) is most commonly used. The viscosity of the contrast medium is sometimes increased by the addition of a thickening powder, which prevents the tendency to alveolar filling and flooding that may occur with the unaltered medium. Following bronchography, as much of the material as possible is recovered by suction. Patients of 12 years or over are most commonly examined by the injection of unmodified Dionosil Oily through the cricothyroid membrane, as previously described (HOLDEN and CRONE 1953). Subsequent recovery of the medium is carried out by supervised postural drainage and coughing (HOLDEN 1957).

Since Dionosil Oily has been used, one of us (R. H. C.) has studied all resected lung tissue from patients previously submitted to bronchography for any evidence of reaction to the presence of foreign material. In addition, a special study was made of the specimens obtained from 49 consecutive patients submitted to lobectomy or pneumonectomy on account of non-tuberculous bronchiectasis over a period of 10 months. The tissue examined included not only the bronchiectatic portions, but normal or near normal areas, which by their anatomical site were inevitably removed. Twenty-one of the patients were male, 28 female. In all, 74 bronchograms had been performed on them: 29 patients had 1, 15 had

2, and 5 had 3 such examinations. The length of time between the bronchograms and operations varied from 1 week to 4 years and the age of the patients ranged from 4 to 41 years, as shown in Diagram 1.

From each specimen, sections of at least 10 paraffin blocks stained by haematoxylin and eosin and Masson's trichrome stain, and a minimum of 3 frozen sections stained by Sudan IV and Sudan Black, were examined. In appropriate cases, sections were also stained by van Gieson's method, orcein, for reticulin by Robb-Smith's modification of Foot's method, and by other fat stains.

In the description of the findings, the term 'fat' is used to describe material occurring in globules or occasionally in small pools, which stains with Sudan IV, Sudan Black, and other ordinary histological stains for fat. No method has been discovered of differentiating arachis oil from endogenous fat in histologic sections. When the fatty material was in small pools and not in spherical droplets it was considered likely that it consisted of arachis oil. It was confirmed that an emulsion of arachis oil takes up these stains in the same way as endogenous fat.

Results

Since 1952 over 2,000 bronchograms have been carried out in these hospitals using Dionosil Oily. As far as can be ascertained, no clinical evidence of long term ill effects has been found in any of these cases. It is unnecessary to discuss further the immediate effects which have been previously recorded (HOLDEN and CRONE 1953, HOLDEN 1955); suffice it to say that any immediate clinical reaction continues to be unusual.

In the survey of all the resected lung tissue the results were necessarily complicated by such reactions as to keratin in the neighbourhood of keratinising squamous carcinomata, and more particularly to endogenous fat in the presence of bronchial obstruction. These reactions were less conspicuous in most cases of bronchiectasis than in cases of pneumonectomy for tumours and some other conditions. Nevertheless, apart from the occasional residuum of arachis oil which had been retained subsequent to recent bronchography, no unusual reaction which could be directly attributed to this examination was noted.

The portions of lung from the 49 cases studied histologically in detail showed changes varying from normal, or near normal, to frankly bronchiectatic areas in which there was considerable bronchial dilatation with peribronchial fibrosis and some peribronchial alveolar collapse. Hypertrophy of smooth muscle around the bronchi and lymphoid hyperplasia with numerous lymphoid follicles were most obvious in younger patients.

Only in 5 cases was there much acute inflammatory change, either in

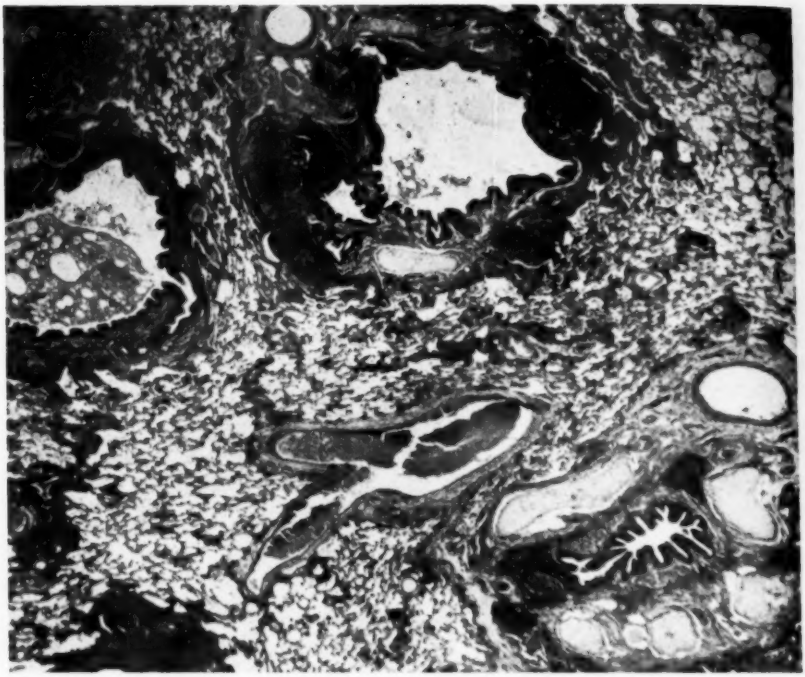

Fig. 1. Section from a bronchiectatic lobe after bronchography on three occasions with Dionosil Oily. (Haematoxylin and eosin.) × 22.

the form of ulcerative bronchitis or small areas of bronchopneumonia. In these, large numbers of organisms were present in the inflammatory exudate. Fat globules were present in grossly dilated bronchi, but without any tissue reaction in their neighbourhood except of acute inflammatory type in keeping with bacterial infection. In each of these cases bronchography had been performed more than 1 month before operation, but no evidence of a granulomatous reaction to foreign material was noted. In a comparable group of lobes obtained at autopsy from patients with infected bronchiectasis, who had not been examined by bronchography, fat droplets of similar size and staining properties were found. Accordingly, there is no evidence to suggest that the acute inflammatory changes recorded can be directly attributed to the contrast medium.

Among the 44 cases with trivial or no inflammatory change, larger droplets or small pools of fatty material, which by their size might be suspected of being arachis oil, were found in dilated bronchi in 5 specimens resected less than 4 weeks after bronchography. Occasional globules were

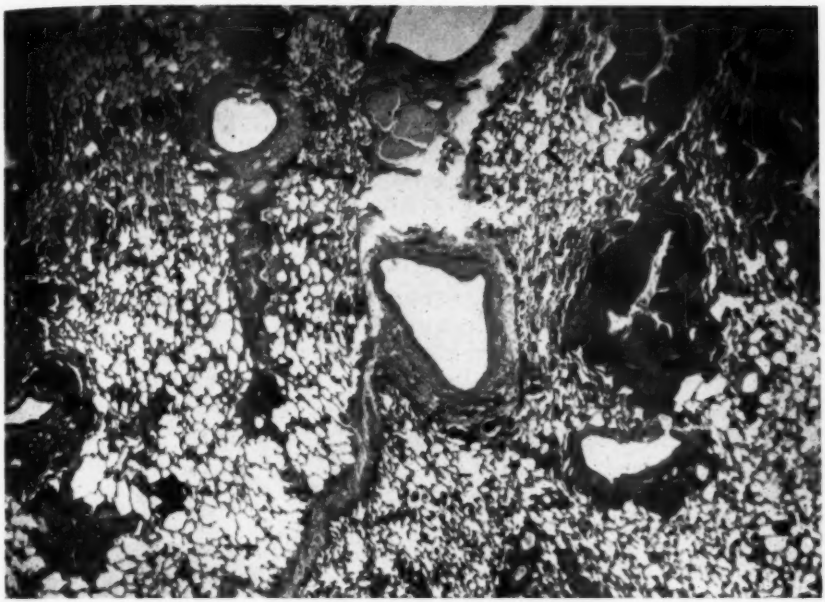

Fig. 2. Section from a bronchiectatic lobe of a patient on whom bronchography had never been performed. (Haematoxylin and eosin.) × 22.

also found in alveolar walls and peribronchial lymphatics. In all cases, with or without acute inflammatory changes, it was possible to find at least some fat droplets in alveolar phagocytes. However, these were also found in bronchiectatic lungs, and are quite often seen in lungs with no gross disease, in which no bronchogram has been performed.

Throughout the series foreign body granulomata of any kind were few, and in no case was fatty material demonstrated in a granuloma. To avoid any confusion, bacteriologically proven cases of tuberculous bronchiectasis were not included in this special investigation. One case showed a granulomatous bronchial lining surrounding an inhaled twig of *Thuja plicata*. Scanty discrete granulomata including giant cells and histiocytes, but with no visible foreign material, were seen in 4 other specimens. They were all near ectatic bronchi, and none was found in the comparatively normal parts of resected lurg. Figs. 1 and 2 show the close similarity of part of a resected lobe from a patient who had 3 bronchograms at intervals of 18, 4 and 3 months before operation and a portion of a lung from an autopsy on a patient on whom bronchography had never been performed. In both there are numerous dense lymphoid aggregates, but no foreign body granulomata.

Discussion

In an earlier report it was recorded that Dionosil Oily was easily administered, well tolerated by the patients and relatively non-irritant (HOLDEN 1955). Nevertheless it is clearly desirable that as much as possible of any foreign material introduced into the lungs should be removed quickly to avoid any tissue reaction. Accordingly, it is considered important to encourage the expulsion of the contrast medium following bronchography by using the available methods such as suction, postural drainage and coughing. Even so, not all the medium can be recovered by these means. Subsequently some is removed along with the bronchial mucus, and is either coughed up or swallowed. Finally, the remainder appears to be absorbed. The propyliodone is excreted by the kidneys, whereas the arachis oil appears to be engulfed by macrophages. This is the route of absorption of vegetable oils as suggested by SANTE (1949). The rate of elimination of the contrast medium is very variable: in most cases the lungs are radiologically clear within 2 days, though occasionally some residuum may remain for longer periods in cases showing bronchial abnormalities.

In their study of the effects of Dionosil Oily in rabbits, BJÖRK and LODIN had the advantage of starting with animals with presumably healthy lungs, and it is reasonable to assume that the oil residua and foreign body granulomata described by them were the results of bronchography. After 3 months oil residua were present in the lungs of 8 out of 10 rabbits, and in 3 there were foreign body granulomata. In 6 months oil residua and granulomata were found in 7 of 10 animals. Both groups showed general thickening of the septa and alveolar walls. Oil was present in the alveoli, alveolar walls, lymphatics and in some of the granulomata. This suggests that during the bronchography alveolar filling and perhaps flooding took place. It is our practice to avoid alveolar filling, and this is generally achieved without difficulty in those examinations carried out under local anaesthesia, while the use of a thickening agent in those cases under general anaesthesia is helpful.

In the present examination of human material it was necessary to study tissue already in part diseased, so that little note can be taken of such changes as thickening of septa and alveolar walls, although no such reaction was noted in otherwise normal lung tissue. It was also not possible to estimate how much of the fatty material observed was arachis oil and how much was endogenous fat. However, it does appear significant that in this human series, the amount of fatty material seen was not very striking, and foreign body granulomata were rare, in fact no more frequent than in similar lungs in which bronchography had not been performed. In addition, no fat staining material was demonstrated in any of the granulomata observed.

HEPPLESTON (1954), in his studies on the fate of inhaled coal dust, observed differences in its effects on the lungs of rabbits compared with man. This he attributes, in part, to the lack of smooth muscle in the respiratory bronchioles of the rabbit which leads to increased pooling and aggregation of the dust particles to an extent not observed in man. It would appear to us that similar effects may occur with Dionosil Oily, thus providing an explanation in part for the apparent differences between man and rabbits, and suggesting the danger of assuming that the results of animal experiment are directly applicable to human disease.

Conclusion

The delayed effects of Dionosil Oily recorded by BJÖRK and LODIN in rabbits have not been substantiated in man. This is probably due to anatomical and physiological differences together with a different technical approach to bronchography, including subsequent recovery of the contrast medium. In the follow-up of human cases the absence of late clinical reactions and the failure to demonstrate any tissue damage has confirmed our previous opinion that Dionosil Oily is a safe and suitable contrast medium for our methods of bronchography.

SUMMARY

Dionosil Oily was used as contrast medium in bronchography in over 2,000 cases without any clinical evidence of long-term ill effects, or deleterious effect on the human lung. Routine histological examinations of all resected lung specimens, following bronchography in the last 5 years, showed no features suggesting any damaging effect of the medium. In resected lung tissue, from 49 patients with bronchiectasis at varying intervals from 1 week to 4 years after bronchography, extremely few foreign body granulomata were revealed, none of which contained fatty material.

ZUSAMMENFASSUNG

"Dionosil Oily" ist als Kontrastmittel bei der Bronchographie in mehr als 2,000 Fällen benutzt worden, ohne dass irgendwelche klinischen Erscheinungen langdauernder Übelkeit oder schädlicher Einwirkung auf die menschliche Lunge auftraten. Die übliche mikroskopische Untersuchung aller resezierten Lungenpräparate von Fällen, in denen während der letzten 5 Jahre eine Bronchographie gemacht wurde, zeigten keine Anzeichen, die auf eine schädliche Wirkung des Mittels hinwiesen. Im resezierten Lungengewebe von 49 Patienten mit Bronchiektasien bei verschiedenen Intervallen von 1 Woche bis zu 4 Jahren, nach der Bronchographie wurden ausserordentlich wenige Fremdkörpergranulome entdeckt; keines von diesen enthielt Fette.

RÉSUMÉ

Le Dionosil 'Huileux' a été utilisé comme moyen de contraste en bronchographie dans plus de 2,000 cas sans aucun signe clinique d'inconvénient à longue échéance ni d'effet nuisible sur le poumon humain. Des examens histologiques systématiques de toutes les piéces d'exérèse pulmonaire, après bronchographie au cours des 5 dernières années, n'ont montré aucun signe pouvant faire penser à un effet nocif de ce produit. Sur le tissu pulmonaire réséqué de 49 malades atteints de bronchectasies, à des intervalles allant d'une semaine à 4 ans après la bronchographie, on n'a trouvé que très peu de granulomes à corps étrangers, dont aucun ne contenait de substance huileuse.

REFERENCES

Björk, L. and Lodin, H.: Pulmonary changes following bronchography with Dionosil Oily (animal experiments). Acta radiol. 47 (1957), 177.

Fischer, F. K.: The bronchial tree: technic of bronchography. *In:* Schinz, H. C. et coll: Roentgen diagnostics, p. 2023. Vol. 3. 1st Amer. Edit. William Heinemann, London 1953.

Heppleston, A. G.: Changes in the lungs of rabbits and ponies inhaling coal dust underground. J. Path. Bact. 67 (1954), 349.

Holden, W. S. and Crone, R. S.: Bronchography using Dionosil Oily. Brit. J. Radiol. 26 (1953), 317.

— Bronchography in pulmonary tuberculosis using Dionosil Oily. Brit. J. Radiol. 28 (1955), 100.

— The behaviour of contrast media in the bronchial tree. Brit. J. Radiol. 30 R(1957), 530.

Sante, L. R.: The fate of oil particles in the lung and their possible relationship to the development of bronchiogenic carcinomata. Amer. J. Roentgenol. 62 (1949), 788.

Werthemann, A. and Vischer, W.: Zur Frage der Lungenveränderungen nach Bronchographien mit carboxymethylcellulosehaltigen Kontrastmitteln. Schweiz. Med. Wchnschr. 81 (1951), 1077.

FROM THE DEPARTMENT OF RADIOLOGY (DIRECTOR: D. MAC RAE), THE MONTREAL NEUROLOGICAL INSTITUTE, MONTREAL, CANADA

THE ROENTGEN APPEARANCES OF THE CAROTID SULCUS OF THE SPHENOID BONE

by

E. P. Engels

On each lateral edge of the superior surface of the basisphenoid there is a broad groove termed the 'carotid sulcus' (4). It forms a sigmoid curve somewhat like the italic letter 'f' above the attachment of each greater wing of the sphenoid. This groove lodges the cavernous sinus and varying portions of the carotid artery, depending upon the age of the individual and consequent varying degrees of tortuosity of the vessel.

COPE has described the ridges and buttresses which may be found on the inner walls of the sphenoid sinuses along the carotid sulcus, thus affording an explanation for the appearance of this structure on the lateral roentgenogram of the skull.

BATSON has described dehiscences in the margins of the carotid sulcus in two skulls by a 'dilating carotid artery'. Thus, in one instance, the bony wall of the sphenoid sinus was eroded, and in another, the dehiscence occurred where the anterior wall of the sulcus bends forward and up under the anterior clinoid process.

The author has frequently noticed in lateral roentgenograms of the skull that all or parts of the margins of the carotid sulcus are visible against the background of the pneumatized sphenoid body. Surprising clarity of the most anterior portion of the sulcus can occasionally simulate

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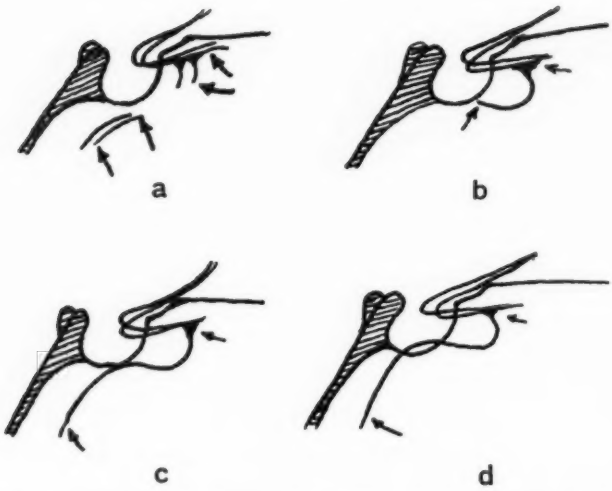


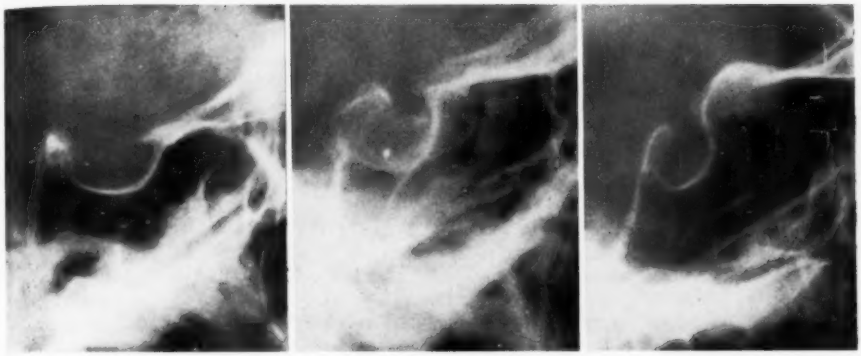
Fig. 1. Schematic representation of some common variations of the carotid sulcus.

the appearance of calcium deposits in the wall of the carotid artery or in an aneurysm. For this reason, and because mention of this structure is not made in most current textbooks of neuro-radiology (3, 5), it was decided to determine the frequency and degree of visibility as well as to note some variations in the appearance of the carotid sulcus in a group of normal skull roentgenograms.

A series of 100 consecutive normal roentgen examinations of the skull in individuals ranging in age from 17 to 66 years were reviewed. In all cases no abnormality had been reported in the region of the sella or in the remainder of the skull.

Common variations in the appearance of the margins of the carotid sulcus appear in Fig. 1. The margins of the entire sulcus on one or both sides were visible in 19 % of individuals as a sigmoid curve (Fig. 1 c). Exceptionally, the margins appeared to rise above the floor of the sella in the horizontal portion of the sigmoid curve (Fig. 1 d).

In the commonest type (Fig. 1 a), triangular-shaped buttresses with small downward linear extensions of the terminal or superior portions of the grooves are shown. Further, small portions of the ascending limbs may or may not be noted. This appearance was found in 26 per cent of the cases reviewed. In 19 per cent, the entire terminal limb of the sigmoid curve was observed (Fig. 1 b). Thus in a total of 64 per cent of all cases, all or part of the sulci on one or both sides could be observed.



a b c

Fig. 2. Roentgenograms demonstrating the variations of the carotid sulcus in three different cases.

The roentgen appearances in three different cases are shown in Fig. 2. Demonstration of both sulci (c) happened in a patient with multiple myeloma, not included in the normal series, in whom no abnormality was found in the sellar or parasellar regions at autopsy.

There was no appreciable sex or age difference in the degree of visibility obtained. The amount of pneumatization of the sphenoid bone and the degree of buttress formation along its inner walls seem to be paramount factors in determining whether this structure was visible or not.

A series of twelve cases of cerebral arteriovenous malformations were reviewed with the intent to demonstrate possible abnormalities in the carotid sulcus. Aside from the fact that this structure seemed quite prominent in some instances, no direct help in diagnosis could be obtained even in retrospect.

SUMMARY

The roentgen appearances and variations of the carotid sulcus of the sphenoid have been described. The frequency, 64 per cent, with which all or parts of this sulcus on one or both sides could be observed should make it an easily recognized landmark in the roentgen examination of the skull.

ZUSAMMENFASSUNG

Das röntgenologische Aussehen und die Variationen des Sulcus caroticus des Keilbeines sind beschrieben worden. Die Häufigkeit (64 %), mit welcher der ganze Sulcus oder Teile desselben auf einer Seite oder bilateral nachgewiesen werden könnten, sollte ihn zu einer leicht erkennbaren Struktur bei der Röntgenuntersuchung des Schädels machen.

RÉSUMÉ

L'auteur décrit les aspects radiographiques et les variations de la gouttière carotidienne du sphénoïde. La fréquence (64 %) avec laquelle on pouvait visualiser partiellement ou totalement cette gouttière d'un côté ou des deux côtés pourrait en faire un repère aisément reconnaissable dans l'examen radiologique du crâne.

REFERENCES

1. Batson, O. V.: Anatomical anomalies of importance to the otolaryngologist. Ann. Otol. Rhin. Laryng. 44 (1935), 939.
2. Cope, V. Z.: The internal structure of the sphenoid sinus. J. Anat. Physiol. 51 (1917), 127.
3. Etter, L. E.: Atlas of roentgen anatomy of the skull. Charles C. Thomas, Springfield 1956.
4. Gray's Anatomy. Thirty-first edition. Longmans, Green, London 1956.
5. Pendergrass, E. P., Schaeffer, J. P. and Hodes, Ph. J.: The head and neck in roentgen diagnosis. Second edition. Charles C. Thomas, Springfield 1956.

FROM THE UNIVERSITY HOSPITAL (DIRECTOR: M. QUINTELA) AND THE MILITARY HOSPITAL, MONTEVIDEO, URUGUAY, SOUTH AMERICA

ANEURYSM OF THE RENAL ARTERY

by

F. Hughes, A. Barcia, O. Fiandra and *J. Viola*

One of us (F. H.) in 1953 reported a case of aneurysm of the renal artery diagnosed by arteriography during operation. We mentioned then that arteriography should permit of a pre-operative diagnosis but that ABESHOUSE was the only one to have reported such a case; the employment of arteriography in the diagnosis of this condition has, however, already been suggested by many authors, as may be seen from the bibliography now included.

Some new observations have recently been published (BEGNER, LJUNGGREN and EDSMAN). Reference is made to a case of a calcified aneurysm of the right renal artery which was confirmed by arteriography. An aneurysm of the lower branch of the artery, which had not been visible in the previous films, was also revealed by the procedure. The investigation of two cases of annular calcifications of the renal parenchyma by means of arteriography forms the subject of our present communication.

Case 1. E. C., aged 55 years, with a 8-year history of increasing pain in the left lumbar region. Conventional roentgenography of the urinary tract showed a semicircular calcification in the region of the left renal pelvis. *Urography* (Fig. 1a) revealed that the calcification lay just above the hilum but outside the pelvis and calyces, which were normal in appearance. There were no changes on the right side and both kidneys functioned normally. Left retrograde *pyelography* confirmed the previous findings. The analysis of

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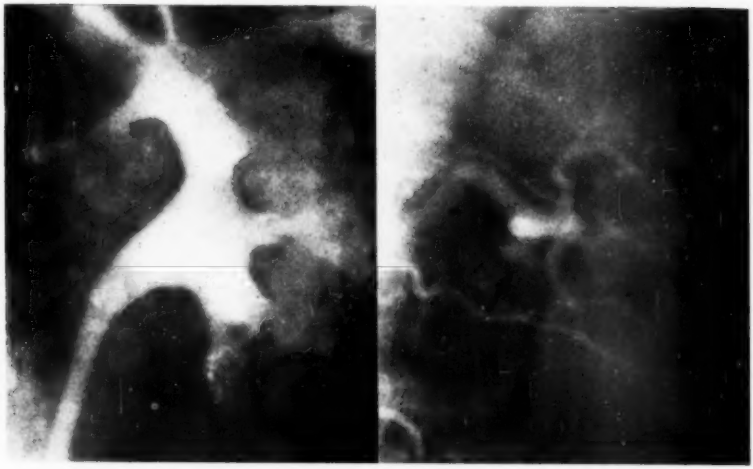

Fig. 1. Aneurysm of the left renal artery. Annular calcification. a) Urography. b) Arteriography.

the urine was normal. *Arteriography* (Fig. 1b) performed by percutaneous catheterization via the right femoral artery, disclosed an aneurysm of the left renal artery at the site of the calcification. The kidney was removed surgically and the examination of the specimen confirmed the arteriographic findings.

Histologic examination (J. F. Cassinelli): Weight of specimen 180 g, size 11 × 5 cm. A saccular dilatation about 2 cm in length and bearing the appearances of an aneurysm was present in one of the branches of the renal artery in the region of the hilum. Microscopy confirmed the presence of a partially calcified true aneurysm caused by arteriosclerosis and atheroma of the artery.

Case 2. C. L. de C., aged 77, with slight hematuria for one month and a history of hematuria together with pain in the left lumbar region a year previously. Cystoscopy revealed no abnormality. At conventional roentgenography of the urinary tract a ring-like density with a transparent centre in the left renal area was observed. Urography revealed that it lay outside the renal pelvis and calyces, which were normal. Arteriography failed to disclose an aneurysm but the doubtful ring-shaped calcification lay close to a branch of the renal artery, suggesting that the calcification possibly lay within the wall of a thrombosed aneurysm.

The cases described emphasize the necessity of locating the site of any calcification in the renal parenchyma by means of arteriography. As stated by VON RONNEN the angiographic study is the ideal method of establishing a diagnosis. It is certain that the more general use of renal arteriography will lead to an increase in the number of cases observed and to the demonstration of aneurysmal dilatations not necessarily calcified. MATHÉ in a survey of 5 cases states that as pain is a dominant

element in the symptomatology of the condition, arteriography should be considered in all cases of persistent renal pain without any apparent signs in the kidney.

SUMMARY

Two cases of aneurysm of the renal artery diagnosed by means of renal arteriography are described.

ZUSAMMENFASSUNG

Zwei Fälle mit einem Aneurysma der Arteria renalis, die mit Hilfe der renalen Arteriographie diagnostiziert sind, werden beschrieben.

RÉSUMÉ

Présentation de deux cas d'anévrysme de l'artère rénale diagnostiqués par artériographie rénale.

BIBLIOGRAPHY

ABESHOUSE, B. S.: Aneurysm of the renal artery: Report of two cases and review of the literature. Urol. cutan. Rev. 55 (1951), 451.

BEGNER, J.: Aortography in renal aneurysm. J. Urol. 73 (1953), 720.

HOWARD, H., SUBY, A. and HERBERSON, J.: Aneurysm of the renal artery. J. Urol. 45 (1941), 41.

HUGHES, F.: Aneurisma de la arteria renal. Documentación arteriográfica operatoria. Arch. esp. Urol. 9 (1953), 83.

LAZARUS, J. and MARKS, M.: Aneurysm of the renal artery, true and false with special reference to preoperative diagnosis. J. Urol. 52 (1944), 199.

LEVINE, B.: Aneurysm of the renal artery. J. Urol. 54 (1945), 17.

LJUNGGREN, E. et EDSMAN, G.: Remarques sur l'artériographie rénale, p. 140. Congr. Soc. Intern. d'Urologie, Athènes 1955. Vol. II.

LOWSLEY, O. and CANNON, E.: Aneurysm of the renal artery. J. Amer. med. Ass. 121 (1943), 1137.

MATHÉ, C. P.: Aneurysm of the renal artery: Report of five cases, one treated by resection of aneurysmal sac without sacrificing the kidney. J. Urol. 60 (1948), 543.

MOREYRA BERNAN, P. y HALAC, A.: Aneurisma de la arteria renal. Rev. argent. Urol. 16 (1947), 88.

VON RONNEN, J. R.: The roentgen diagnosis of calcified aneurysms of the splenic and renal arteries. Acta radiol. 39 (1953), 385.

SELDINGER, S.: Catheter replacement of the needle in percutaneous arteriography. Acta radiol. 39 (1953), 368.

SHARP, R. and GREEN, M.: Diagnostic and therapeutic considerations in renal aneurysm with a report of two additional cases. J. Urol. 64 (1950), 214.

FROM THE DEPARTMENT OF RADIOLOGY (DIRECTOR: PROF. CARL WEGELIUS) AND THE SURGICAL CLINIC (DIRECTOR: PROF. A. R. KLOSSNER), TURKU UNIVERSITY, TURKU, FINLAND

ROENTGEN EXAMINATION OF THE AFFERENT JEJUNAL LOOP AND DUODENUM AFTER PARTIAL GASTRECTOMY — BILLROTH II

by

Seppo Kajas

A patient who has been subjected to a Billroth II resection may be examined by means of a barium meal. It is generally found that the part of the afferent jejunal loop which extends from the site of the enteroanastomosis to the duodenum as well as the duodenal stump are not filled with contrast medium. Since, however, in a good many cases the patient is suffering from gastric symptoms in spite of the fact that no gastrojejunal lesion is apparent, it is evident that the method of examination cannot be considered entirely satisfactory.

The disadvantage is particularly marked in examinations after operations of the exclusion type, or after resections which for one reason or another are regarded as inadequate.

RIBBING (1951) relieved the obstruction of the efferent jejunal loop by a Miller-Abbot tube, after which it was possible to fill the afferent loop with contrast medium given by mouth. RIBBING gave no details of the roentgenologic findings.

Because this procedure is somewhat complicated, the author has made attempts to fill the afferent loop by some easier method.

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Fig. 1. Filling of the afferent jejunal loop and duodenum through a stomach tube introduced in the afferent loop.

Methods

Two different procedures were employed. In the first method a stomach tube, longer than the normal, was introduced into the afferent loop under fluoroscopic control. Contrast medium was then introduced into the loop under moderate pressure, the injection being carefully watched upon the fluoroscopic screen. The contrast medium was diluted barium emulsion.

The alternative technique was a simpler one. After the patient had swallowed a suitable amount of the emulsion, he lay on his right side and was subjected to fluoroscopic control. The afferent loop and duodenum were outlined in about every fourth case. The fluoroscopic examination had often to be continued for a considerable time and the roentgenograms were obtained immediately when the contrast medium was observed to have filled the duodenal stump; if attention was paid to this latter point it was found that the rapid flow of the medium into the coils of the small intestine might mask the region under examination.

A retrograde motion of a contrast medium in the small intestine is possible even if it has been introduced the usual way and, in the author's opinion, may occur in routine examinations. That the afferent loop is not generally filled in the course of an ordinary examination depends

largely on the fact that this part of the bowel is not given special attention and the fluoroscopic observation is not continued long enough. Out of a material of 50 examinations, the author managed to fill the afferent jejunal loop and the duodenum in 15 cases. In 5 the first method was used, and in the remainder the second was employed. A typical example is illustrated in Fig. 1.

SUMMARY

Two different methods of filling the afferent jejunal loop and the duodenum in patients with partial gastrectomy ad modum Billroth II are discussed.

ZUSAMMENFASSUNG

Zwei verschiedene Methoden, die afferente Jejunalschlinge und das Duodenum bei Patienten mit partieller Gastrectomie ad modum Billroth II zu füllen, werden besprochen.

RÉSUMÉ

L'auteur étudie deux méthodes différentes pour remplir l'anse jéjunale afférente et le duodénum chez les malades qui ont subi une gastrectomie partielle type Billroth II.

REFERENCES

RIBBING, S.: Röntgenundersökning av den tillförande slyngan efter operationer enligt Billroth II. (Swedish.) Svenska LäkT. 48 (1951), 1781.

VIIKARI, S. J. and KLOSSNER, OLLI: The primary and late results of 1,050 partial gastrectomies for chronic gastroduodenal ulcer. A clinical study. Acta chir. scand. Suppl. 220 (1956).

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PENDULOUS FLAT CASSETTES IN PANTOMOGRAPHY

by

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In accordance with the principles of pantomography a flat film moving linearly, or a rotating bent film, sharply reproduce that layer (a pantomogram) of the moving object which passes the narrow vertical roentgen ray beam with the same linear velocity as the surface; the latter is of course stationary in relation to the film. All other parts of the object move at a different speed and cannot, therefore, be projected sharply onto the film.

It is possible to obtain a pantomogram of any stratum with a rotating bent film (1, 2, 4), although in practice a thin layer is always selected, but when the film moves linearly (3) only vertical surfaces, curved or flat, can be reproduced.

In the first instance, the film is held on a horizontal disc-like film holder which is rotated by a horizontal annular object holder of the same size and at the same angular velocity (2, 4). Hence, all points equidistant from the rotational axes pass the narrow roentgen ray beam with the same linear velocity, and a constant relationship is thus maintained.

Experiments with pendulous flat cassettes have given so good results that a publication of the theory and practical application of the technique appears to be justified.

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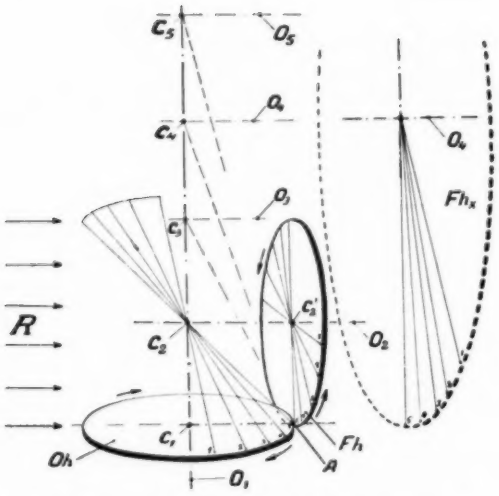

Diagram 1. Pantomography with film holders rotating about the horizontal axis.

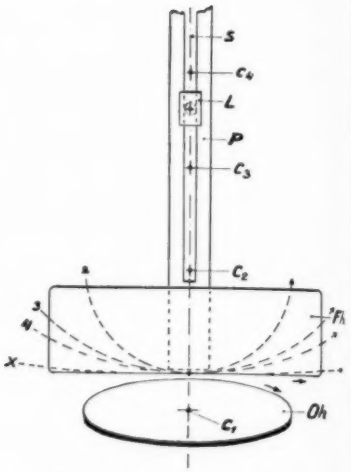

Diagram 2. Pantomography with pendulous cassettes.

Let us assume that the disc-shaped film holder (*Fh*) has been tilted upwards (Diagram 1) about its contact point (*A*) with the object holder (*Oh*). The rotational axis (O_2) of the film holder is now situated perpendicularly to the rotational axis (O_1) of the object holder, and the film holder can be rotated about the horizontal axis.

The diameter of both holders is equal. The angular velocity of the holders is thus the same because the object holder by reason of the friction between the edges of the discs makes the film holder rotate with it. Hence, the principles of the pantomographic method apply also in this case.

Despite the divergence of roentgen rays, it is assumed for the sake of simplicity that the roentgen beam (*R*) consists of parallel rays which are also parallel with the axis (O_2). Accordingly, the rays are perpendicular to the surface of the film holder (*Fh*), whose rotational centre is (C'_2). The roentgen film may be attached to the front or back surface of the film holder in a flat cassette or envelope in such a manner that the film surface is parallel with the disc.

If an object is now positioned on the object holder (*Oh*) and the object holder is rotated about its centre (C_1) on the axis (O_1), two conical surfaces are projected onto the film. The sectional point (C_2) of the axis is the common vertex of the cones, the base of the upper cone being

upwards. After a rotation of 360° there will be a double projection onto the film and it is therefore better to turn the disc through only 180°, and thus obtain a reproduction of the upper cone on one half and the lower cone on the other half of the film. Only semi-cones of each will of course be obtained. But if the object is not higher than the radius of the film holder, the system can be rotated through 360°, and a reproduction of the whole conical surface, the vertex of which will lie at the point C_2, will appear in the film. It is assumed in the diagram that the discs have been rotated through only 80°. The outline of the conical surface on the object holder and its projection onto the film holder (and the film) are marked with lines, numbered 1, 2, 3, 4, and 5, respectively. The arrows show the rotational direction of the holders.

The height of the conical surface may be changed by altering the size of the film holder. The larger the radius of the film holder, the higher will be the conical surface reproduced in the film and the less will the conical surface differ from a vertical cylindric surface. If the rotation point of the film holder is at infinity the surface reproduced is for all practical purposes cylindric.

The diagram shows how the form of the conical surface changes when the size of the film holder is increased two, three, or four times. Lines O_3, O_4 and O_5 denote the corresponding axes and points C_3, C_4 and C_5 the corresponding vertices. The slotted oblique lines from these points show the inclination of the conical surface in each case. When the radius of the film holder (Fh_r) is three times as great as the original radius, the projection of the conical surface differs considerably from the original.

It will have been noted that by altering the length of the radius of the film holder the height of the conical surface to be roentgenographed can be altered. In addition, the form of the conical surface may be changed by altering the mutual speed of the holders. If the velocity of the object holder is kept constant, the angular speed of the film holder may be altered. If the speed is altered during the exposure, the reproduction is not that of a regular conical surface. Hence, by changing both the speed and the radius of the film holder during the exposure it is actually possible to obtain a pantomogram of any kind of surfaces situated at any depth. Even spherical layers may be reproduced, as ordinary flat films can be used — within certain limits — in pantomography of such layers (6). As far as the control of the film speed is concerned, various recognized mechanical arrangements may be employed. For instance, a roller system as used in pantomography with linearly moving flat cassettes (3), or a modification of it, may be found suitable.

If the swinging movement of the cassette is controlled without friction between the film holder and the object holder, a simple pendulum can

Fig. 1. Pantomogram of a conical layer taken with a pendulous flat cassette. Facial part of a dry skull.

be used for carrying the cassette, as shown in Diagram 2. In practice, the flat cassette (*Fh*) may be attached to the pendulum (*P*), the rotational axis of which may be raised or lowered by moving the slide (*L*) in the slit (*S*). If the turning point of the pendulum is, for instance, C_2, the lowest point of the latter moves alongside the slotted circle 2; this circle corresponds to the periphery of the object holder (*Oh*). The slotted circle (3) corresponds to the rotation axis (C_3), etc. The higher the slide, *L*, is situated, or in other words the larger the rotational radius of the pendulum (film holder or cassette), the less does the turning circle of the lower end of the pendulum differ from a straight line. The circle X corresponds to a radius equal to 20 times that of the object holder. If the radius of the object holder is 14 cm, as in our apparatus, the length of the pendulum is about 280 cm. Thus an ordinary room is high enough to accomodate a pendulum of sufficient length to make pantomography of flat surfaces practicable. In such a case the pendulum technique corresponds to the linearly moving flat cassette technique.

Stereoscopy may also within certain limits be employed. The less the conical surface differs from a vertical surface, the larger will be the area of the surface that can be seen tri-dimensionally at one time.

Fig. 1 is a conical reproduction of a dry skull showing the posterior part of the nasal cavity and the maxillary sinuses. The rotational radius of the pendulum was about 20 cm.

SUMMARY

The theory and the practical application of pendulous cassettes in the pantomography of flat and conical surfaces is presented. If the pendulum to which the flat cassette is attached is sufficiently long, the method is similar to the one in which a linearly moving flat cassette is employed.

ZUSAMMENFASSUNG

Die theoretische und praktische Anwendung pendelnder Kassetten bei der Pantomographie flacher und konischer Oberflächen wird vorgelegt. Wenn das Pendel, an dem die flache Kassette befestigt ist, lang genug ist, dann ist die Methode derjenigen, bei der eine sich linear bewegende flache Kassette benutzt wird, ähnlich

RÉSUMÉ

L'auteur expose la théorie et l'application pratique de cassettes pendulaires pour la pantomographie de surfaces planes et coniques. Si le bras pendulaire auquel la cassette plane est fixée est assez long, la méthode devient semblable à celle où on utilise une cassette plane avec un déplacement rectiligne.

REFERENCES

1. Paatero, Yrjö, V.: A new tomographical method for radiographing curved outer surfaces. Acta radiol. 32 (1949), 177.
2. — Pantomography in theory and use. Acta radiol. 41 (1954), 321.
3. — The principles of the construction and function of the stereo-pantomograph. Acta radiol. 43 (1955), 113.
4. — Die Anwendung der Pantomographie für klinische Untersuchungen. Fortschr. Röntgenstr. 82 (1955), 525.
5. — Kartiopintojen muodoista stereopantomografiassa (Finnish). Suom. hammaslääk. toim. 52 (1956), 145.
6. — Pantomography of spherical layers. Acta radiol. 48 (1957), 181.

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OVARIAN FUNCTION AFTER COMBINED SURGICAL AND RADIOLOGIC TREATMENT OF EARLY CERVICAL CANCER

by

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The loss of ovarian function is a very important and serious sequela in irradiation treatment of cancer of the uterine cervix in young women. In advanced stages of the disease, the prognosis is so grave that this sequela must be disregarded and the patient be given as effective irradiation treatment as possible. In patients with a small, apparently localized cancer of the portio vaginalis attempts have been made to replace irradiation therapy with electrocoagulation, amputation of the cervix, etc., but these measures have proved to be inadequate.

In December 1949 we decided to try if it was possible, in selected cases, to protect the ovaries against the radiation effect by moving them, prior to the irradiation, from their normal site in the small pelvis and fixing them as far away from the irradiated field as possible without impairing the blood supply.

Similar experiments did not seem to have been reported in the literature, but later BATTEN and BROWN (1956) published a case in which the ovaries were successfully protected during postoperative irradiation treatment of a neuroblastoma of the pelvis in an eight-year-old girl.

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At laparotomy, enucleation of the tumour was abandoned, but the ovaries were lifted as high as possible, attached to the parietal peritoneum and ensheathed in lead shells which were removed surgically after the irradiation treatment (total dose 2,150 r given in 30 days).

An experiment performed by one of us (KREBS 1928) gives an idea of the distance from the uterus at which ovarian tissue is damaged during radium treatment for cancer of the cervix. Tumour tissue (mammary carcinoma from mice) enclosed in small sterile rubber capsules was placed in the uterine cavity, between the uterus and the ovaries, and at a distance of 6 cm from the uterus in an autopsy specimen of the female internal genitalia. Radium was then applied for 36 hours by the method used at that time, while the specimen was stored at a temperature of about + 10° C.

Subsequent transplantation into suitable mice gave no takes of the tumour tissue from the uterine cavity, a distinctly reduced percentage of takes of the tumour tissue previously placed just outside the uterus, but a normal number of takes (about 95 %) of the tumour tissue which had been placed at a distance of 6 cm from the uterus of the specimen; a control material (tumour tissue placed in the same room 3 to 4 m from radium) showed the same percentage of takes.

Obviously, we were rather hesitant about the planned therapeutic experiment. In particular, we were in doubt as to what effect the preserved ovarian function and the production of ovarian hormones would have, if the experiment proved successful, on the prognosis of a form of genital cancer such as cancer of the cervix compared with that in markedly hormone-dependent genital cancers such as cancers of the breast and prostate.

The problem was whether the preserved ovarian function would be beneficial or detrimental to the result of the treatment of the cervical cancer, or if it possibly would be without any significance.

Material and Methods

The case material consisted of 18 patients who applied for treatment at the Anti-Cancer Centre during the period from 1 December 1949 to 30 November, 1950. With the exception of 4 patients (1 with a severe psychosis; 1 who was about four months pregnant, and in whom abortion was induced and followed by severe complications; 1 who had recently been operated on for an extra-uterine pregnancy; and 1 who had undergone bilateral salpingo-oophorectomy), all patients under 40 with cervical cancer in Stage I were included in the series. In addition to these patients (13 in all), a few patients in Stages II and III were also subjected

to ovarian lifting because it was desirable to gain an impression of the effect of the intervention on the result of irradiation treatment.

By now, the length of the observation periods is from 6 to 7 years in all the patients.

We have adhered to the clinical classification by stages (Heyman), *i. e.* a given case was still designated as being in Stage I, even if it was recognized at operation that it had been incorrectly classified.

After the conclusion of the usual clinical examination (the taking of a careful history, gynaecologic examination, histologic examination of biopsy specimens, cystoscopy, electrocardiography, etc.) the patient was subjected to operation.

An inferior midline laparotomy was performed. The ligament of the ovary was divided and the ovary with the infundibulo-pelvic ligament mobilized, care being taken that the blood vessels of the ovary were left intact. The ovary was then lifted up and fixed with silk-knot sutures to the margins of a small incision into the parietal peritoneum on the psoas muscle or retroperitoneally to this muscle, so that the ovary occupied a position above the linea terminalis of the pelvis. The distance between the cancer of the portio and the lower pole of the ovary was usually 13 to 15 cm, in a few cases up to 18 cm. The salpinx was removed only in exceptional cases, generally if it presented signs of chronic inflammation.

Unilateral lifting of the ovary was performed in 7 and bilateral lifting in the remaining 11 cases.

Five to eight days postoperatively, radium or combined radium and roentgen therapy was instituted. The patients who received radium therapy alone were treated as follows: Radium was applied twice at an interval of 10 days, each time for 24 hours, in a tube (60 to 70 mg) placed in the cervical canal and in a box (70 to 100 mg, depending on the size of the portio) placed in the vagina against the tumour.

In the patients who were given combined radium and roentgen treatment, the following technique was used: Four or five days postoperatively roentgen irradiation was commenced through two anterior fields (10 × 10 cm), two posterior fields (15 × 10 cm) and a perineal field. The entire dose to each anterior field was 2,400 r, 150 r daily through a Thoræus filter (0.4 mm Sn), distance 50 cm, voltage 165 to 180 kV; the entire dose to each posterior field was 1,800 r and to the perineum 1,000 r, the total dose thus being 9,400 r. Radium was applied for the first time 10 days after the commencement of roentgen irradiation and for the second time after another 10 days. When, after about two months, the entire treatment was completed, the patient was allowed eight days of rest in the hospital — a feature which in our opinion is of great value.

At the roentgen treatment of the patients in whom ovarian lifting

had been performed we were very careful in avoiding irradiation of the ovaries. The beam of roentgen rays was, as far as possible, directed downwards, away from the new site of the ovaries, but as will appear from the following account this was not sufficient to avoid damage to these organs.

If radium therapy is given in the usual way, ovaries placed in their normal site will receive about 3,600 r in 24 hours. If, as in the present cases, the ovaries are moved to a distance of about 14 cm, the dose received will be about 90 r in 24 hours, *i. e.* about 1/40 (NIELSEN 1938).

Results

Stage I. Ovarian lifting was performed in 9 patients, whose ages ranged from 22 to 37 years and averaged 29.5 years. After the lapse of 6 1/2 years, 8 were alive without signs of recurrence, whereas 1 died from recurrent cancer 12 months after the treatment.

By way of comparison it may be mentioned that during the preceding two years (1948—1949), a total of 24 patients under 40 years with cervical cancer in Stage I were treated with combined radium and roentgen therapy. Of these, 18 were alive after 6 years, while 6 had died; after the lapse of 7 years, 1 more died and cancer recurred in another patient. Thus, cure was obtained in two-thirds of these patients (in 16 out of 24).

A comparison of these small groups of patients do not suggest that ovarian lifting has aggravated the prognosis.

Stage II. Ovarian lifting was performed in 6 patients. After the lapse of 6 1/2 years, 4 were alive and well, without any signs of recurrence at the follow-up examinations.

During the preceding two years, we had treated 30 patients of the same age-group suffering from cervical cancer in Stage II. Of these, 13 died of the cancer and 2 of unknown causes (possibly cancer). The figures are limited, but here, too, they suggest that the intervention has not aggravated the prognosis.

Stage III. Ovarian lifting was performed in 3 patients, aged 22, 27 and 31 years. Of these, 1 is alive and well after the lapse of 6 1/2 years.

Table I shows the results in the patients who were treated with combined radium and roentgen therapy. It is seen that menstrual function was not preserved in any of these patients in spite of the fact that attempts had been made to place the irradiated fields and direct the beam of roentgen rays below the site of the ovaries.

Table II shows that menstrual function was preserved in 6 of the 8 patients who had been given radium therapy alone. The two in whom

Table I

Menstruation in surviving patients after ovarian lifting and combined radium and roentgen therapy

Stage	Age	Ovarian lifting	Distance in cm	Menstruation
I	37	Bilateral	12	Ceased
I	35	Unilateral	13	»
I	32	Bilateral	15	»
II	36	Unilateral	13	»
III	29	»	15	»

Table II

Menstruation in surviving patients after ovarian lifting and radium therapy

Stage	Age	Ovarian lifting	Distance in cm	Menstruation
I	24	Unilateral	13	Preserved
I	22	Bilateral	12	»
I	35	»	14	»
I	34	»	14	Ceased
I	23	»	13	Preserved
II	35	»	15	»
II	29*	»	13	»
II	39	»	14	Ceased

* Six years later pregnancy terminating in abortion at fourth month.

the menstruation ceased were: a woman, aged 39, who seemed to pass into a premature menopause, and another, aged 34, in whom postoperative ileus developed, necessitating renewed laparotomy with separation of adhesions and removal of one of the ovaries.

In order to illustrate the condition in the six patients in whom menstrual function was preserved after curative radium therapy the case histories are briefly reported.

Case reports

Case 1. Married woman, aged 24, with cervical cancer, Stage I. Menstruation had always been slightly irregular. Ovarian lifting was performed on 16 December 1949, and the postoperative course was uneventful. Radium therapy was given. On 7 December 1950 the patient was re-admitted to the Department of Surgery with pain in the left iliac fossa. Palpation revealed a hazelnut-sized mass above the left inguinal ligament.

Laparotomy showed that the right ovary was small and atrophic, without corpus luteum formation. The patient had just had her menstruation. The left ovary revealed

a cyst, the size of a hen's egg, which was removed, while the remaining, apparently normal, ovarian tissue was preserved. (Histologic diagnosis: Follicular cyst of the ovary.)

During the 6 1/2 years which have elapsed since the second operation she has had menstrual bleedings, appearing at slightly irregular intervals and lasting from 3 to 11 days. On two occasions menstruation failed to appear for 2 to 3 months. During these periods she had hot flushes, which disappeared when the menstruation recurred.

At the last follow-up examination (27 July 1957), inspection revealed a small portio vaginalis; the external os was distinctly seen. There was slight atrophy of the mucosa around the portio, while normal wrinkled mucosa was noted in the vagina, which was 9 cm in depth. The patient stated that she has marital coitus once or twice weekly with perfectly normal sexual gratification.

Case 2. Unmarried woman, aged 22, with cervical cancer, Stage I. Bilateral ovarian lifting was performed on 14 March 1950, and the postoperative course was uneventful. Radium therapy was given. Shortly after the surgical intervention and the completion of the radium therapy, menstruation recurred and continued regularly without molimina.

At the last follow-up examination (30 July 1957), the patient looked perfectly healthy; the breasts were well developed, and tender prior to expected menstruation. She stated that she has sexual intercourse almost every day, with perfectly normal orgasm. The labia appeared normal; the portio was slightly flattened. The vagina measured 9 cm in depth and showed a normal degree of moisture. Rectovaginal examination showed no abnormalities.

Case 3. Divorced woman, aged 35, with cervical cancer, Stage I. Both ovaries were lifted on 5 August 1950, without postoperative complications. Radium therapy was given. The patient menstruated normally during the first six months after the operation, but then menstruation ceased, possibly due to early onset of the menopause; characteristic hot flushes and sweats developed, but these decreased in intensity during the last year. The patient felt well.

This patient was given a relatively high dose of radium irradiation, because the portio was very large. A box with 100 mg radium was placed against the portio, as distinct from the other patients in whom only 70 to 80 mg was used. Obviously, it is difficult to say if this may have been a contributory cause of the early menopause.

At the last follow-up examination (10 August 1957), the vulva appeared normal, and the portio was of normal form and size; external os of normal appearance; no mucosal atrophy. The degree of moisture was practically normal; the depth of the vagina was 9 cm. Rectovaginal examination showed no abnormalities.

The patient stated that up to one year ago she had had coitus twice weekly, with normal orgasm.

Case 4. Married woman, aged 23, with cervical cancer, Stage I. Ovarian lifting was performed on 2 November 1950, without postoperative complications. Radium therapy was given. During the 7 years which have passed since the operation, the patient has been perfectly well. Menstruations regular, appearing at fortnightly intervals and lasting 1 to 2 days. The patient has sexual intercourse with her husband, but from which she has never derived any pleasure, either before or after the operation. Her breasts were tender before the onset of the menstrual bleeding.

At the last follow-up examination (30 July 1957), the vagina was normally moist; the portio was flattened. The introitus of the vagina was torn posteriorly. The vaginal mucosa appeared normal; the vagina measured 8 cm in depth.

Case 5. Married woman, aged 35, with cervical cancer, Stage II. Bilateral ovarian lifting was performed on 21 March 1950, without postoperative complications. Radium therapy was given. During the 7 years which have passed since the operation, the patient has menstruated normally, and she has had normal marital relations. During the

last few months (the patient is now 43) the menstrual flow has decreased and mild hot flushes have developed. She still had intercourse once weekly, with normal orgasm.

At the last follow-up examination (31 May 1957), slight atrophy at the top of the vagina was noted. The portio was small and atrophic. The depth of the vagina was 9 to 10 cm; the mucosa was wrinkled and soft, and the vaginal walls were of normal appearance. Rectovaginal examination revealed normal conditions.

Case 6. Married woman, aged 29, with cervical cancer, Stage II. Bilateral ovarian lifting was performed on 24 June 1950, without postoperative complications. The patient suffered from severe mental depression both before and after the onset of the disease. She had been treated with electroshock on three occasions. Regular menstruations of normal intensity, appearing at intervals of 21 to 24 days and lasting 6 to 7 days. Just as before the operation, she experienced a sensation in the breasts before menstruation although this had decreased during recent years. Menstruation never failed to appear, except 2 years ago when pregnancy intervened, terminating in abortion at fourth month. Her husband is often away on business, but she had sexual intercourse with him two or three times monthly, with orgasm of the same intensity as before the onset of the disease. No hot flushes or sweats.

At the last follow-up examination (30 July 1957), the labia and portio were found to be normal. The vagina measured 7 cm in depth. The patient had her menses at the time of the examination. Rectovaginal examination showed normal conditions.

In connexion with the 18 ovarian liftings there has only in one case been complications which were directly referable to the intervention.

A married woman, aged 34, with cervical cancer, Stage I. Bilateral ovarian lifting was performed on 11 October 1950, together with routine appendectomy. On the seventh postoperative day, mechanical ileus developed. Re-operation revealed that the small intestine was adherent to and twisted on the floor of the pouch of Douglas. The left ovary showed haemorrhagic infarction; the right ovary was of normal appearance. The intestinal adhesions were separated and the left ovary was removed; the postoperative course was then uneventful.

One year later total hysterectomy and bilateral oophorectomy were performed in another hospital. This operation revealed haematometra and gland cells of the corpus uteri suggestive of cancer. The patient was then well for some time, but was admitted to hospital in 1954 for suspected ileus. In 1957 she was re-admitted with chronic subileus. A portion of the jejunum was resected and some adhesions were separated. No signs of carcinosis or recurrence; no vaginal bleeding since the radium therapy.

Discussion

The follow-up examinations after observation periods of almost 7 years and the analysis of this limited case material seem to show:

1. The ovarian lifting as such and the preserved ovarian function have not had any detrimental effect on the results of the irradiation treatment of cervical cancer.

2. Ovarian lifting does not result in preserved menstrual function in patients who are subsequently given combined radium and roentgen therapy.

3. The menstrual function was preserved in 6 of the 8 patients who were given radium therapy alone. Six years after the treatment, one of these patients became pregnant, but had an abortion at the fourth month.

Thus, in most cases it seems possible, without aggravating the prognosis, to avoid premature menopause induced by the irradiation therapy in young women with early cervical cancer who can be treated with radium alone. From the limited experience so far gained it may be said that the benefit which these patients derive from the treatment is a matter of opinion. The case histories reported suggest that these young women may be spared considerable psychic and somatic difficulties. The local sequelae and discomfort caused by the irradiation treatment seem to be diminished; the subsequent sexual lives of the patients are undoubtedly facilitated and rendered more normal. The distressing symptoms usually accompanying a premature menopause are, to a great extent, avoided.

Note added in proof

From 1 August 1957 we have again begun to perform ovarian lifting in young women suffering from cervical cancer in Stage I or II. Table III shows that in 7 out of 8 patients menstruation recurred after the radium therapy. No complications were encountered in this group.

Table III

Menstruation in surviving patents after ovarian lifting and radium therapy

Stage	Age	Ovarian lifting	Distance in cm	Menstruation
I	38	Bilateral	17	Ceased
Ij	35	»	13.5	Preserved
		(diabetes)	8.5	
I	23	Bilateral	12	»
II	36	»	12	»
I	36	»	13	»
I	33	»	13	»
I	33	»	13	»
I—II	31*	Unilateral	14	»

* Right-sided salpingo-oophorectomy.

SUMMARY

In six out of eight young women with early cervical cancer, premature menopause from curative radium treatment was avoided by an operation in which one or both ovaries were lifted to a distance of at least 13 cm from the tumour. On the other hand, this intervention did not result in the preservation of ovarian function after combined radium and roentgen therapy. Neither the intervention nor the preserved ovarian function seemed to detract from the results obtained by the irradiation treatment of the malignant condition.

ZUSAMMENFASSUNG

Bei 6 von 8 jungen Frauen mit kleinen Zervixkarzinomen wurde eine vorzeitige Menopause durch kurative Radiumbehandlung vermieden, in dem man das eine Ovarium oder beide Eierstöcke operativ in mindestens 13 cm Abstand vom Tumor brachte. Andererseits ergab dieser Eingriff keinen Schutz für die Ovarialfunktion nach kombinierter Radium- und Röntgenbehandlung. Weder der Eingriff noch die bewahrte Ovarialfunktion scheinen die Resultate, die durch die Strahlenbehandlung der bösartigen Erkrankung erreicht werden, zu verringern.

RÉSUMÉ

Chez six sur huit jeunes femmes atteintes de cancer du col au début, on a pu éviter une ménopause curiethérapique anticipée grâce à une opération par laquelle un ou les deux ovaires ont été remontés à une distance d'au moins 13 cm de la tumeur. Par ailleurs, cette intervention n'a pas permis de préserver la fonction ovarienne après association curiethérapique et roentgenthérapique. Ni l'intervention ni la préservation de la fonction ovarienne n'ont paru diminuer la qualité des résultats du traitement radiothérapique de cette affection maligne.

REFERENCES

BATTEN, R., and BROWN, D. E. M.: Protection of ovaries from radiation. Lancet 1956: I, p. 939.

KREBS, C.: Experimental studies concerning the radiologic treatment of cancer uteri. Acta radiol. 9 (1928), 1.

NIELSEN, B.: Nogle tilfælde af cancer uteri undersøgt med hysterografi med henblik paa betingelserne for radiumbehandling (Danish). Ugeskr. Læger 28 (1938), 790.

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DETERMINATION OF SODIUM AND PHOSPHORUS IN HUMAN CERVICAL MUCUS WITH ACTIVATION ANALYSIS

by

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Earlier studies have shown considerable variation in the percentage of the dry substance in the human cervical mucus (BERGMAN 1950 and the authors' unpublished data). This percentage (w/w) has ranged from about 2 to about 14 in different samples depending on the phase of the menstrual cycle or pregnancy during which they are recovered. It may be of interest to determine what elements or chemical compounds are mainly responsible for these extreme variations in the dry weight of cervical mucus. BERGMAN (1950) and IGASHARI (1954) have claimed that the NaCl concentration in the cervical mucus is relatively constant. RYDBERG (1948) discussed the possibility of a variation in the NaCl contents. The publication of BERGMAN and LUND (1950) indicated that the osmotic pressure of cervical mucus does not show such extensive variations as the dry substance but remains at a fairly constant level. (Freezing point depression about 0.52° C in follicular phase and about 0.65° C in luteal phase.)

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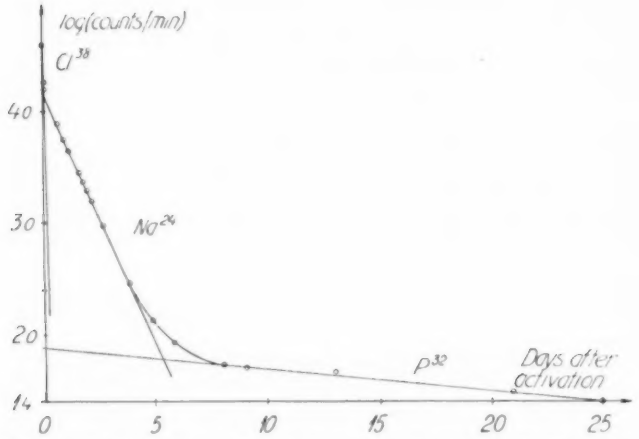

Diagram 1. Typical example of a decay of activated sample. The curve can be resolved into Cl^{38} (+ N^{13}), Na^{24} and P^{32} components.

In view of these reports we decided to examine the Na and P contents in human cervical samples, and due to the minute amounts of material available we selected activation analysis for this purpose. The nuclear reactions utilized were Na^{23} (d, p) Na^{24} and P^{31} (d, p) P^{32}.

Technique

The technique was similar to one employed by two of the present authors (O. & M.) in the activation analysis of P^{31} in histologic sections. Samples of human cervical mucus weighing 5 to 15 mg were placed on thin aluminium foils dried and incinerated below + 400° C, so that their thickness on the average was about 200 $\mu g/cm^2$. The samples were thus very thin and easily penetrated by the deuteron beam of the cyclotron (of about 6.5 MeV) having a maximum range of about 50 mg/cm^2 of Al. The aluminium foils carrying the samples were mounted on a rotating disc which was irradiated to an accumulated dose of about 0.1 μAhr ($= 2 \times 10^{15}$ deuterons) per specimen. After finishing the activation the samples were counted repeatedly in a G. M. counter and decay curves were drawn and resolved in components corresponding to Na^{24} and P^{32} activities. There was also a short-life activity, probably Cl^{38} (37 min), arising from the Cl^{37} (d, p) Cl^{38} reaction with an admixture of N^{13} (10 min), arising from the C^{12} (d, n) N^{13} reaction. The activities extrapolated to zero time of this activation (Diagram 1), were

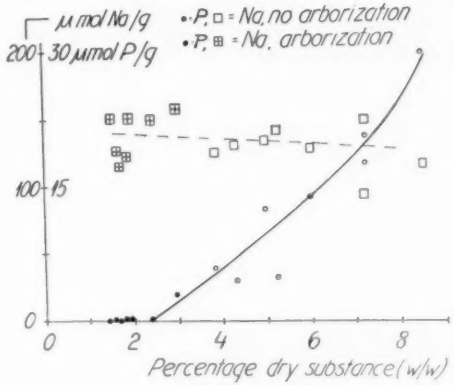

Diagram 2. Na and P contents in cervical samples having different percentages of dry weight (w/w).

obtained and corrected with the empirical geometry factor of the G. M. tube to obtain the original decay rates. With the aid of the formula

$$\frac{\triangle n}{n} = \sigma \cdot M \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (1)$$

where $\triangle n/n$ is a fraction of the reacting deuterons, σ is the (d, p) reaction cross-section in cm^2 and M is the number of target nuclei per cm^2 in the specimen; this last quantity could be calculated. As cross-sections at 6.5 MeV were used:

for the Na^{23} (d, p) Na^{24} reaction $= 0.45 \cdot 10^{-24}$ cm^2, and

for the P^{31} (d, p) P^{32} reaction $= 0.07 \cdot 10^{-24}$ cm^2.

For details of the calculation the reader is referred to a previous paper (ODEBLAD 1956).

Discussion of results

The results are collected in Diagram 2. They show the amount of Na and P as a function of the percentage dry weight of the sample. The values for Na are relatively constant and independent of the percentage of dry substance while the amount of P is directly correlated to the amount of dry substance.

Our results support the view that the sodium chloride concentration remains at about a constant level throughout the menstrual cycle and suggest that the variations in the amount of dry substance is due mainly to the organic constituents (some of which contain phosphorus) of the

cervical sample. Further, since phosphorus usually has an intracellular location, the determinations of P may afford a rough indication of the contents of cellular elements within the sample.

It is apparent that the midcycle secretion contains very small amounts of phosphorus. It is also evident that the disappearance of arborization with a high percentage of dry substance cannot be attributed to the lack of sodium chloride but to other factors.

SUMMARY

The technique for the determination of the sodium and phosphorus in human cervical mucus is described. The amount of Na was found to be relatively constant but the amount of P was directly correlated to the amount of dry substance.

ZUSAMMENFASSUNG

Die Technik, welche zur Feststellung von Natrium und Phosphor im menschlichen Zervikalschleim benutzt worden ist, wird beschrieben. Der Natriumgehalt war relativ konstant, während der Phosphorgehalt in direkter Beziehung zur Menge der Trockensubstanz stand.

RÉSUMÉ

Les auteurs décrivent une technique de mesure de la teneur en sodium et en phosphore du mucus cervical humain. Ils ont trouvé une teneur en Na relativement constante, mais une teneur en P directement en relation avec la teneur en substance sèche.

REFERENCES

Bergman, P.: Sexual cycle and time of optimum fertility in woman. Acta Obstet. gynec. scand. 1950, Suppl. 4.

— and Lund, C. G.: The osmotic pressure of human cervical mucus. Acta Obstet. gynec. scand. 30 (1950), 267.

Igashari, M.: Studies on the cyclic changes in human cervical mucus as well as its crystallization. J. Jap. Obstet. gynec. Soc. 1 (1954), 194.

Odeblad, E.: Activation analysis with charged particles. Acta radiol. 45 (1956), 396.

Rydberg, E.: Observations on the crystallization of the cervical mucus. Acta Obstet. gynec. scand. 28 (1948), 172.

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STEROL SYNTHESIS AFTER WHOLE BODY ROENTGEN IRRADIATION

III. Effects of synkavit

by

H. K. Hanel, G. Hjort and *P. R. Purser*

In continuation of our previous work (1) on the synthesis of cholesterol from 2-C^{14}-acetate, we have studied the effects of methylnaphthohydroquinone alone and in conjunction with whole body irradiation.

MITCHELL et coll. (2, 3) have studied various substances which increase the sensitivity of living organisms to ionising irradiation. One of the best-known of these is the tetra-sodium salt of 2-methyl-1,4-naphthohydroquinone-diphosphate, known as synkavit. Treatment with this compound before irradiation is known to increase the mortality of rats.

Experimental

We used the same experimental techniques as described in our previous publication (1).

The animals, male DLB mice, 6 to 7 weeks old, were divided into four groups. The first, control, group received no treatment before injection of 20 μc 2-C^{14}-acetate intraperitoneally. The second group received 400 r whole-body roentgen irradiation followed by acetate injection immediately, 1 day, 3 days, and 7 days after irradiation. The third

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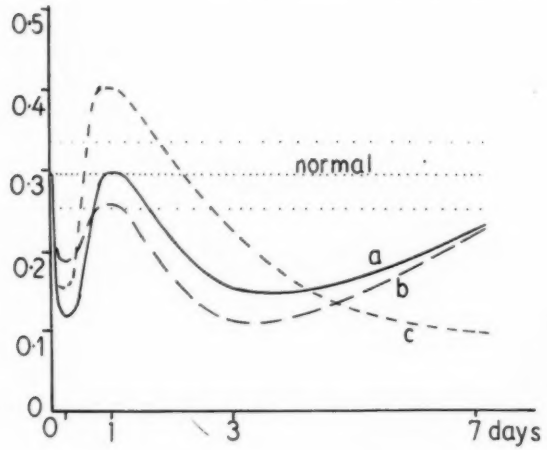

Diagram 1. Cholesterol concentration in mg/g liver after treatment with: a — synkavit followed by 400 r whole-body irradiation; b — synkavit alone; c — radiation alone. The normal level and its standard deviation are also shown.

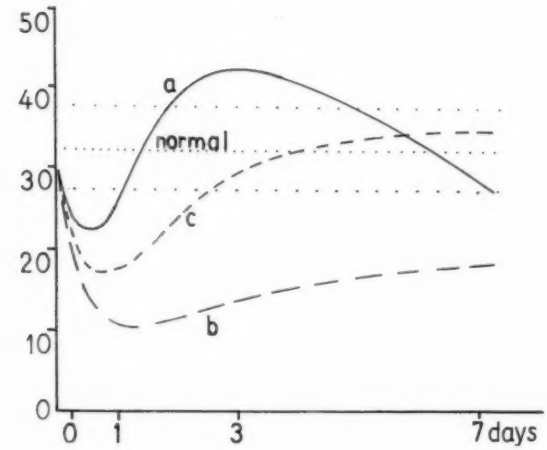

Diagram 2. Synthesis rate of liver cholesterol from 2-C^{14}-acetate, as shown by the activity of the synthesised cholesterol in c/m/g liver, after treatment with: a — synkavit followed by 400 r whole-body irradiation; b — synkavit alone; c — radiation alone. The normal level and its standard deviation are also shown.

group were injected intraperitoneally with 2 mg (0.2 ml of a solution of synkavit 'Roche') followed by acetate injections at the same time intervals. Group four were given the synkavit injection followed after 20 minutes by 400 r whole-body roentgen irradiation and subsequent acetate injections. The animals were killed by decapitation 6 hours after the acetate injection, the livers taken out and processed as previously described.

Discussion of results

The results of the investigation are shown in Tables 1 and 2, and in Diagrams 1 and 2.

The synthesis rate shows a decrease during the first day after treatment in all three groups and increases again after 1 day. We find it difficult to

Table 1

Cholesterol concentration in mouse liver after treatment with synkavit and roentgen-irradiation. Figures are given as mg cholesterol/g liver

Treatment	Time after treatment			
	6 hours	1 day	3 days	7 days
None-controls	0.293 ± 0.035			
Synkavit	0.073 ± 0.033	0.259 ± 0.049	0.110 ± 0.037	0.215 ± 0.033
Radiation	0.154 ± 0.025	0.404 ± 0.065	0.225 ± 0.036	0.098 ± 0.030
Synkavit + radiation	0.117 ± 0.017	0.295 ± 0.071	0.154 ± 0.019	0.221 ± 0.056

Table 2

Activity of cholesterol synthesised from 2-C^{14}-acetate in mouse liver after treatment with synkavit and roentgen irradiation. Figures given as c/m/g liver

Controls	32.4 ± 5.8			
Synkavit	22.6 ± 2.4	10.6 ± 2.0	13.9 ± 2.6	17.9 ± 3.4
Radiation	23.2 ± 5.3	17.2 ± 4.2	29.3 ± 6.7	34.8 ± 10.8
Synkavit + radiation	23.8 ± 6.2	25.5 ± 2.3	53.8 ± 6.5	28.1 ± 7.8

In all, 132 mice were used.

explain the fact that the combined treatment, synkavit plus irradiation, gives a smaller effect than either of the single treatments.

The cholesterol concentration, or pool size, similarly shows the same disturbances in all three groups; a rapid decrease in the first six hours, a maximum at 1 day and a subsequent decrease. In this case the initial disturbance is greater for the combined treatment than for either of the single treatments. By comparison of the graphs of synthesis rate and pool size, it seems reasonable to deduce that the break-down of cholesterol is minimal at 1 day and maximal at three days after treatment in all three groups.

The results definitely show that in its effect on cholesterol synthesis synkavit is radiomimetic.

Histologic examination of the liver cells of synkavit-treated animals shows bridge formation, chromatin clumping and pyknotic nuclei, similar to the abnormalities observed in radiation treated animals, as illustrated in our previous paper (1), but no vacuolisation of cell nuclei was observed in animals treated with synkavit alone. The number of cells affected was less than 1 %.

Acknowledgements

The authors wish to thank Miss K. Høegh and Mr. M. Poulsen for valuable technical assistance.

SUMMARY

The authors have shown that the tetrasodium salt of 2-methyl-1,4-naphthohydroquinone diphosphate (synkavit), in the concentration used, is radiomimetic in its effects on cholesterol synthesis from sodium acetate in mouse liver. Histologic examination of the liver cells shows changes in the nuclei and mitotic figures in a few of the cells.

ZUSAMMENFASSUNG

Die Verfasser haben gezeigt, dass das Tetranatriumsalz des Synkavits in der angewandten Konzentration radiomimetisch auf die Cholesterolsynthese aus Natriumazetat in der Mäuseleber einwirkt. Histologische Untersuchung der Leberzellen zeigt in einigen wenigen Zellen Veränderungen der Kerne und der Mitosen.

RÉSUMÉ

Les auteurs ont montré que le sel tétrasodique du diphosphate de 2-méthyl-1:4-naphtohydroquinone (synkavit) à la concentration utilisée est radiomimétique par ses effets sur la synthèse du cholestérol à partir de l'acétate de sodium dans le foie de la souris. L'examen histologique des cellules hépatiques montre des modifications des noyaux et des figures de mitose dans un petit nombre de cellules.

REFERENCES

1. Hanel, H. K., Hjort, G., Johansen, G. and Purser, P. R.: Sterol synthesis after whole-body roentgen irradiation. I. Cholesterol synthesis from 2-C^{14}-acetate in mouse liver in vivo. II. Cholesterol synthesis from 2-C^{14}-acetate in rat liver in vitro. Acta radiol. 48 (1957), 227.
2. Mitchell, J. S.: Histological changes produced by large doses of tetra-sodium 2-methyl-1:4-naphthohydroquinone diphosphate in some human tumours. Experientia 5 (1949), 293.
3. — Clinical assessment of tetra-sodium 2-methyl-1:4-naphthohydroquinone diphosphate as a radiosensitiser in the radiotherapy of malignant tumours. Brit. J. Cancer 7 (1953), 313.

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LOCATION AND DURATION OF RETENTION OF RADIOACTIVE PARTICLES IN MICE

by

Bo Holma and *Arne Nelson*

Investigations on the penetration, retention, and ultimate fate of inhaled aerosol particles are of great interest from the aspect of industrial hygiene. The air pollution problem which has appeared with the fast development of the peaceful use of atomic energy as well as its military application has furthermore emphasized the importance. In this connexion it seems to be of interest to investigate the correlation between the size of particles, and the site and duration of retention in different organs after inhalation. Earlier investigations have been carried out but none of the methods used have clarified the problem sufficiently.

Theoretical work on the retention of aerosols in the respiratory system (FINDEISEN 1935, HATCH and HEMEON 1948, and LANDAHL 1950), calculated as a function of the size of particles, inertia, sedimentation, wall-effect, and Brownian movement, has been published. Most experimental investigations refer to the total retention without any differentiation between the different parts of the lungs. This work has generally been carried out by means of polydisperse aerosols.

In earlier investigations the extent of retention has been recorded by analyses of the concentration of particles, partly in exhaled air, which was

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collected in different fractions, to obtain a measure of the depth of penetration, and partly from different parts of the respiratory system. In these studies, chemical analyses, conventional histologic staining technique, and autoradiography were used.

The site of retention has been determined in mice by various kinds of oils (SHOSHKES, BANFIELD and ROSENBAUM 1950). A conventional histologic technique was employed. Spores of B. subtilis marked with P^{32} have also been used in mice in order to determine the percentage retention of the distribution of particles of 0.5 μ radius (HARPER and MORTON 1953). The number of spores in the various organs were calculated by comparing the radioactive and viability counts in tissues in which they were contained.

A theoretical analysis based on earlier experimental data has shown that particles with a radius of 0.5 μ have the highest alveolar penetration (HATCH and HEMEON 1948). Theoretical calculations show the highest retention in the alveoli with particles of 0.3 μ radius (FINDEISEN 1935, and LANDAHL 1950). The size of the aerosol particles, among other factors, is of great importance for the depth of penetration in the respiratory system. An attempt has been made to determine the alveolar retention in man after the inhalation of a radioactive monodisperse aerosol by measuring the activity with a Geiger-Müller counter placed on the thoracic wall (WILSON and LAMER 1948). No experimental investigation, however, has been carried out under physiological conditions in the attempt to obtain definite knowledge of the site of the retention of particles with regard to the particle size. It is necessary to work with monodisperse aerosols, to use a registration method in which the washing-away of particles as in most histologic techniques is avoided, and sacrifice the animals in a way that prevents the sources of error which arise if the lungs collapse or if the ciliary activity in the respiratory tract does not cease to function immediately after death.

The present investigations have been made in the attempt to fulfil these demands.

Method

A monodisperse aerosol was prepared by an apparatus originally designed by RAPAPORT and WEINSTOCK (1955) and modified to suit the purpose of this investigation; this apparatus makes it possible to produce aerosols with a desired particle size. The range of particles from a classic LAMER apparatus is 0.08 to 3 μ radius. An investigation is now in progress to determine the range of particle sizes which can be obtained with our modification of the apparatus of RAPAPORT and WEINSTOCK. The raw

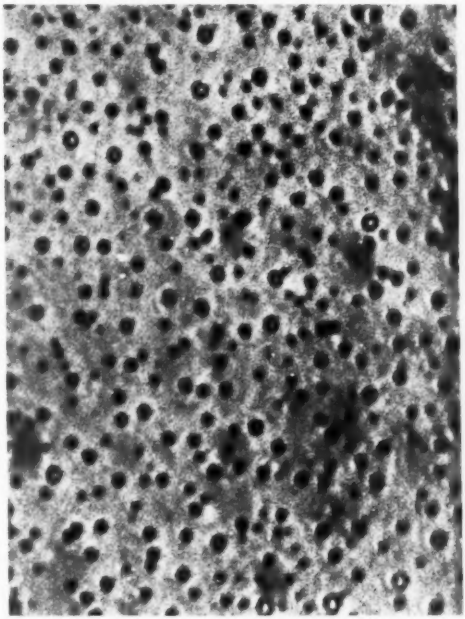


Fig. 1. Sample of aerosol.

material of the aerosol was tricresylphosphate, labelled with P^{32}. This substance is insoluble in water and has a specific weight of 1.2 g/ml.

Before entering the aerosol generator the air passed through a glass-fibre filter. The flow rate, which was 6 liters air/min, was measured with a manometer at the outlet side of the exposure chamber which was made of plexiglass and had a volume of 21 liters. The aerosol concentration in the exposure chamber was registrated by measuring the weight difference of a glass-fibre filter at the outlet before and after a known volume of air had passed. The size of particles were determined before, during, and after every exposure at the outlet of the exposure chamber by means of a 'high-order Tyndall spectrum'. The various measurements were in good agreement [$M_r = 0.38\ \mu$ (M_r = number median radius); $\sigma_r = \pm 0.06\ \mu$]. Samples of the aerosol (Fig. 1) were also collected on slides by the method of thermal precipitation for measuring the size of the particles by a microscope. The cover glasses used for the precipitation were treated with silicone. The flattening out of the drops were taken into account.

Investigations made in this institute indicate that the large radius observed macroscopically should be multiplied by a factor of 0.64 to ob-

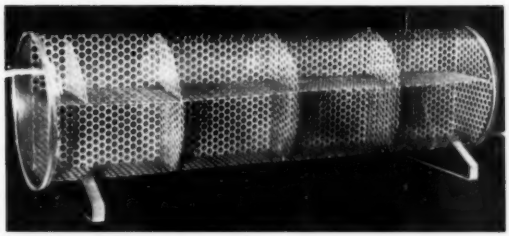


Fig. 2. Exposure chamber.

tain the true radius. Thus the corrected value will be $M_r = 0.41\ \mu\ \sigma_r = \pm 0.06\ \mu$. The activity of the aerosol was 3.7 mc/g ($1.2 \cdot 10^{-9}$ μc per particle).

Young white mice were used as experimental animals. They were placed on perforated shelves in the exposure chamber (Fig. 2) with every mouse in a separate enclosure.

The animals were exposed to the aerosol for one hour and killed at various intervals after the exposure by immersion in a freezing mixture of acetone, alcohol and carbonic acid snow at a temperature of $-90°$ C. After freezing, the animals were transferred in Dewar receptacles to a cold storage room at $-12°$ C, where they were allowed to dry for 24 hours. They were then fixed on bakelite plates with moistened cotton wool, which was frozen with carbonic acid snow, and cut into sections, 20 μ thick. The sections were collected on tape according to ULLBERG (1954) (Fig. 3) and dried for another 24 hours in the cold storage room before being placed in a hermetically closed receptacle for restoration to room temperature. Autoradiography was then carried out by placing the tapes with the sections directly on the films (Dentus Rapid) and leaving them in presses for 2 to 3 months.

Results

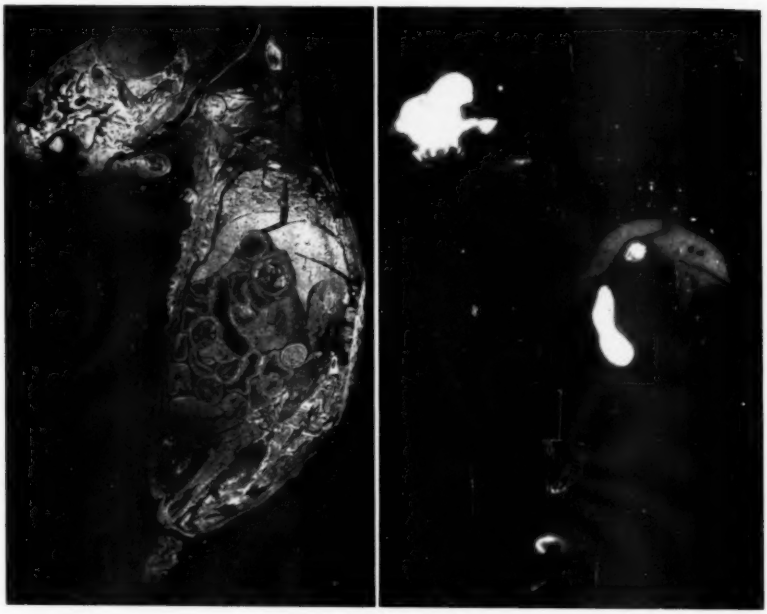
Figs. 4 and 5, from a series of autoradiographic films from mice sacrificed immediately, 5 min, 120 min, one day, and two days, after exposure to radioactive aerosol, show the distribution of the radioactivity. Immediately following the exposure, marked density in the films corresponding to the nose, mouth and stomach, with somewhat less density over the lungs and bronchi, was apparent; over the liver, kidneys and bladder the density was less. Mice killed 5 minutes later showed the same distribution but the density in the lungs had adready decreased. Sixty minutes after the exposure there was nothing left in the lungs, only a little in the

Fig. 3. Sectioning, with tape, of the mouse embedded in cotton wool.

mouth and the nose, and rather more in the kidneys and bladder. The stomach had still the same density but there was now some density corresponding to the intestines. After 120 minutes the stomach and the intestines still showed the same degree of density but in the other regions it had decreased. One day after the exposure the stomach was completely and the intestines, liver, and kidneys almost clear. The urinary bladder showed a rather marked density, and density now appeared in the skeleton. The density in the intestines represents the resorption in the walls. Two days after the exposure the distribution was the same.

It is apparent from the autoradiograms that the retention of particles with a radius of 0.35 μ takes place in the upper respiratory tract and down to the bronchi. It is, however, possible that some particles reached the more peripheral parts of the lungs, although in an amount insufficient to affect the films. The main part of the inhaled aerosol lies in the stomach where the concentration is already high after five minutes; the density then passes on to the intestines. The ciliary activity in the nose seems to clear this organ fairly quickly. In some cases the activity remains longer in the oral cavity due to repeated intake caused by the animals licking their coat. The lungs also show rapid clearing caused by ciliary movement; 60 minutes after the exposure there is no activity corresponding to any site in the lungs.

In spite of the low solubility of the aerosol in water, part of it is digested as shown by the increased density in the intestinal wall, liver, kidneys, bladder and skeleton.



a b

Fig. 4. a) Tissue section (20 μ) of mouse sacrificed immediately after exposure to radioactive aerosol. b) Autoradiogram of the tissue section.

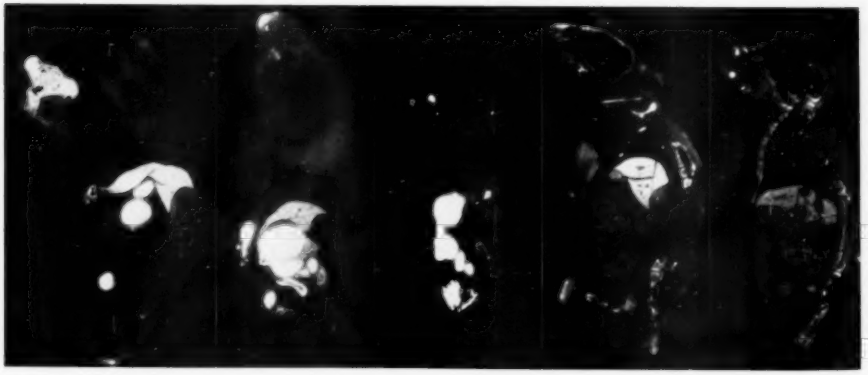


Fig. 5. Autoradiograms of sections of mice: 5 min, 60 min, 120 min, 1 day, and 2 days, respectively, after exposure to radioactive aerosol.

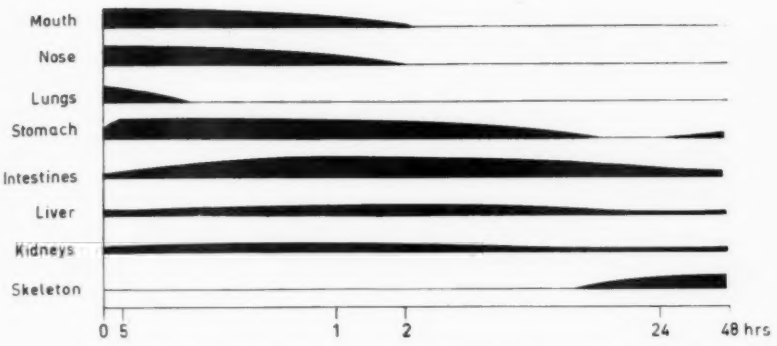


Diagram 1. Distribution of activity in different organs in mice after termination of inhalation of tricresylphosphate aerosol, labelled with P^{32}, particle radius 0.38 μ.

In Diagram 1 an attempt has been made to plot the distribution of the activity in the different organs against time periods following the exposure.

Discussion

The ciliary epithelium in the lungs of mammals transports particles towards the larynx at a speed of 3 to 4 cm/min. It is therefore necessary to cut off this activity instantaneously if particles which have penetrated deeply into the lungs are to be localized. The lung should not be allowed to collapse if phagocytosis is to be investigated. HULSE (1955) of Harwell has demonstrated the difference in the position of cells containing dust particles in lungs which have collapsed and in lungs which have not collapsed post mortem.

Particles which have not had time to undergo phagocytosis may be washed away or changed in position during fixing, embedding, and staining. Optical measurements do not permit of the registration of particles with a radius of less than 0.1 μ, which can be performed by autoradiography.

The use of radioactive aerosols, and the sacrificing of the animals by immersion in a freezing mixture and 'tape cutting' forms a method by which most difficulties can be avoided. A disadvantage of the method lies in the difficulty of cutting 10 μ thickness sections of porous lung tissue, which must necessarily be embedded. There are also always the risks that the particles may be dissolved, altered in position, or washed away. The use of insoluble fluorescent particles may offer a solution to the latter problems although it must be remembered that such aerosols will be polydisperse.

An aerosol produced according to RAPAPORT and WEINSTOCK has an electric charge, but which would probably be discharged by the radioactivity if employed as in our technique.

Water-soluble substances will be retained and recognized by our method, but if the freezing of the animals is not rapid enough large crystals will be formed and the cells destroyed; it is essential that the freezing mixture should be fluid at the body temperature of the animals.

Acknowledgements

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SUMMARY

A method is described by which the location and the duration of retention of inhaled particles were recorded under physiologic conditions by the exposure of mice to a radioactive aerosol, the mice being subsequently sacrified, sectioned, and autoradiographed. The distribution of the aerosol is discussed.

ZUSAMMENFASSUNG

Eine Methode wird beschrieben, bei der die Lokalisation und die Retentionszeit inhalierter Partikel unter physiologischen Bedingungen nach Exponierung von Mäusen mit radioaktivem Aerosol registriert wird. Die Mäuse werden dann getötet, und hergestellte Schnitte werden autoradiographiert. Die Verteilung des Aerosols wird diskutiert.

RÉSUMÉ

Description d'une méthode par laquelle la localisation et la durée de la rétention de particules inhalées ont été étudiées dans des conditons physiologiques par l'exposition de souris à un aérosol radio-actif; les souris ont été ensuite sacrifiées, et les sections preparées ont été autoradiographiées. La répartition de l'aérosol est étudiée.

REFERENCES

FINDEISEN, W.: Über das Absetzen kleiner in der Luft suspendierter Teilchen in der menschlichen Lunge bei der Atmung. Pflügers Arch. ges. Physiol. 236 (1935), 367.

HARPER, G. J. and MORTON, J. D.: The respiratory retention of bacterial aerosols; experiments with radioactive spores. J. Hyg. (Lond.) 51 (1953), 372.

HATCH, T. and HEMEON, W. C. I.: Influence of particle size in dust exposure. J. indust. Hyg. 30 (1948), 172.

HULSE, E. V.: A concept of dust in the lungs. J. Path. Bact. 69 (1955), 225.

LANDAHL, H. D.: On the removal of air-borne droplets by the human-respiratory tract: I. The lung. Bull. Math. Biophysics 12 (1950), 43.

PALMGREN, A.: Tape for microsectioning of very large, hard or brittle specimens. Nature 174 (1954), 76.

RAPAPORT, E. and WEINSTOCK, S. E.: A generator for homogeneous aerosols. Experentia 11 (1955), 363.

SHOSHKES, M., BANFIELD JR., W. G. and ROSENBAUM, S. J.: Distribution, effect and fate of oil aerosol particles retained in the lungs of mice. Arch. industr. Hyg. 1 (1950), 20.

ULLBERG, S.: Studies on the distribution and fate of S^{35}-labelled benzylpenicillin in the body. Acta radiol. (1954) Suppl. 118.

WILSON, I. B. and LAMER, O. K.: The retention of aerosol particles in the human respiratory tract as a function of particle radius. J. industr. Hyg. 30 (1948), 265.

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ENVAHISSEMENTS GANGLIONNAIRES INGUINO-ILIO-PELVIENS PAR LYMPHOGRAPHIE

par

J. M. Collette

Localisations particulières d'un cancer généralisé ou métastases d'un cancer localisé, les adénopathies iliaques sont toujours reconnues tardivement. Jusqu'à présent, en effet, aucune technique d'exploration directe de cette chaîne ganglionnaire n'a été décrite.

La démonstration radiologique de la voie lymphatique périphérique chez l'homme a fait l'objet de deux travaux distincts. Dès 1936, SERVELLE, par ponction directe, souvent percutanée, de canaux lymphatiques très dilatés met en évidence la lymphostase de certains éléphantiasis. KINMONTH (1955) décrit une technique radiologique pour mettre en évidence le réseau lymphatique superficiel du membre inférieur, par intubation directe d'un tronc périphérique.

Expérimentalement, nous avons démontré que la mise en évidence des troncs lymphatiques préganglionnaires est suivie, le plus souvent de l'opacification des relais ganglionnaires correspondants et de leurs troncs efférents.

La chaîne ganglionnaire iliaque externe étant le relais commun des efférents des ganglions inguinaux et de la plupart des lymphatiques pelviens, il nous a paru que la mise en évidence de ces voies lymphatiques profondes pouvait être obtenue à partir de l'injection d'un tronc sous-cutané périphérique du membre inférieur.

Soumis à la Rédaction le 29 Mars 1957.

Technique

Dans sa méthode, KINMONTH obtient l'opacification du réseau lymphatique superficiel par injection dans un canal lymphatique du pied, d'un dérivé iodé hydrosoluble. Afin d'en faciliter le repérage et l'intubation, le canal lymphatique est préalablement coloré par le Patent Blue Violet (P.B.V.) (diéthyl-N') (N'amino) — (2'' sulfonate, 4'' sulfonyl, 53 hydroxyédiéthyl N — fuchsonimine). Cette substance, injectée dans le tissu cellulaire sous-cutané provoque très rapidement une coloration bleu intense des troncs lymphatiques de drainage. Le P.B.V. est dépourvu de toxicité et, contrairement à d'autres colorants lymphatiques, est rapidement éliminé en totalité par les reins.

Nous avons repris essentiellement la méthode de KINMONTH en l'adaptant aux conditions particulières de la démonstration du groupe ganglionnaire inguino-ilio-pelvien.

Repérage d'un tronc lymphatique périphérique. Nous intubons de façon systématique, un lymphatique superficiel de la face dorsale du pied. Ce choix, apparemment paradoxal, présente deux avantages: la facilité d'accès, condition essentielle à la réussite de cette opération minutieuse et l'obtention d'une réplétion ganglionnaire plus homogène et plus étendue en surface. En effet, en raison de la division dichotomique des troncs lymphatiques périphériques, l'opacifiant progresse dans des voies parallèles, de plus en plus nombreuses qui atteignent simultanément les premiers relais ganglionnaires.

L'injection lente du P.B.V. est faite dans le tissu cellulaire sous-cutané de la face externe du gros orteil. Les troncs de drainage sont visibles sous la peau dans les 10 minutes qui suivent l'injection du colorant.

Incision et dissection. La zone d'incision est choisie au niveau d'un trajet lymphatique linéaire longitudinal, en aval de la jonction de deux troncs afférents; elle est anesthésiée par infiltration de xylocaïne.

On procède ensuite à une incision longitudinale d'un centimètre et demi à deux centimètres et à une dissection prudente du derme et du tissu cellulaire sous-cutané. Le tronc lymphatique, isolé, est minutieusement dégagé de sa gaine lâche fibroconjonctive. Ce dégagement est important, car la plupart des fausses routes sont dues au fait que l'injection est poussée dans la gaîne et non dans le canal lymphatique lui-même.

Intubation. Le lymphatique est clampé en amont et tendu par une légère traction sur pince. L'aiguille, de calibre très fin (No 26), adaptée à un raccord en polythène (P. E. 10), est introduite dans la lumière du vaisseau sur une distance de 0,5 centimètre environ, longueur nécessaire et suffisante pour serrer les mords d'une petite pince en deça du biseau sur le trajet intubé.

Injection du produit de contraste et prise des clichés. Pendant que l'opérateur maintient rigide le complexe fragile du lymphatique et du matériel d'intubation, un aide injecte le produit de contraste au moyen de seringues à débit réduit. Le produit utilisé est un composé hydrosoluble tri-iodé à 76 % (solution aqueuse complexe du sel de sodium et de methylglucamine de l'acide N.N'— diacetylamino-triiodobenzoïque — Urografine Schering). Dans certains cas cependant, surtout lorsqu'il s'agit de conditions circulatoires défavorables, on peut obtenir des images lisibles en utilisant un tri-iodé à 60 %. La vitesse d'injection est d'environ 1 ml toutes les 15 secondes. La quantité minimale est de 7 ml. Nous injectons le plus souvent 12 ml.

Il existe un intérêt manifeste à suivre la réplétion de la chaîne ganglionnaire; aussi, dès l'injection des deux premiers ml, nous prenons 7 clichés du bassin, à intervalles de 30 secondes environ: le dernier étant réalisé en incidence oblique.

Fig. 1. Démonstration du réseau lymphatique pré-ganglionnaire (1) du relais (2) et des efférents (3) après injection souscutanée d'Umbradil 50 (2 ml) dans le tissu cellulaire sous-cutané de la patte antérieure du lapin.

Les inconvénients du procédé sont:

1. Une coloration gris-bleu des téguments qui persiste de 24 à 48 heures après l'injection: passé ce délai, la totalité du colorant a pratiquement été éliminée.

2. Une sensation douloureuse qui apparaît le long du trajet lymphatique et au niveau des relais ganglionnaires inguinaux. L'intensité de la douleur est très variable; négligeable chez les uns, très intense chez les autres, elle s'atténue très rapidement et disparaît dès la fin de l'injection. Cet inconvénient constitue cependant pour l'opérateur un test de réussite de l'intubation.

3. Durant les deux premières années d'expérimentation de la technique, nous avons utilisé divers produits de contraste di- et tri-iodés et dans 1/3 des cas, nous avons observé un retard de cicatrisation de la zône d'incision. Bien que spontanée, elle fut précédée d'une nécrose aseptique locale s'étendant longitudinalement sur 2 à 3 centimètres. Deux patients ont présenté des complications septiques (lymphangite).

Depuis l'emploi systématique du produit de contraste mentionné plus haut, nous n'avons plus observé de complication.

Pour autant que l'on se limite aux quantités mentionnées, notre expérience actuelle s'étendant sur 100 lymphographies et lymphadénographies, ne nous a pas montré d'autres inconvénients.

L'injection de plus grandes quantités du produit de contraste est dangereuse: en effet, le produit de contraste altère progressivement la perméabilité des troncs lymphatiques et il se produit une diffusion autour de ceux-ci dans le tissu cellulaire sous-cutané, qui ne tolère pas une telle concentration.

Le changement de perméabilité des troncs lymphatiques rend d'ailleurs inutile l'injection de quantités importantes: après 15 ml environ, l'exsudation du produit de contraste est totale et il ne se produit plus aucune progression centripète.

Fig. 2. Lymphatique de la face interne du membre inférieur suivant le trajet de la saphène.

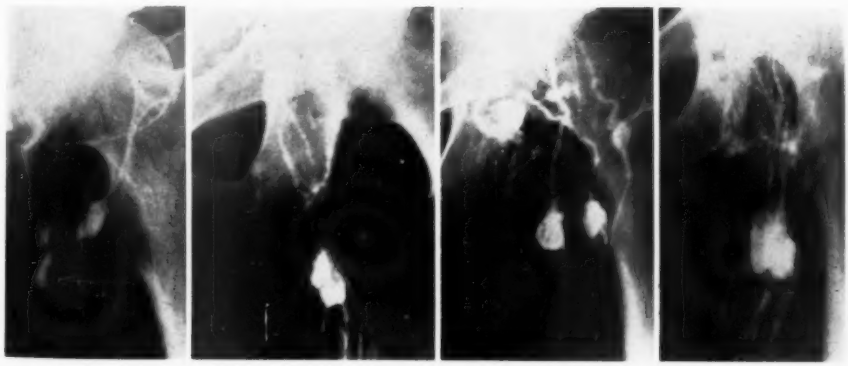

Fig. 3. Images ganglionnaires normales. Les afférents abordent le sinus directement ou après division «en pinceau». La réplétion se fait de façon homogène du sinus vers le hile.

Fig. 4. Lymphadénogramme normal. Deux ganglions inguinaux superficiels mis en évidence (1), leurs efférénts passent partiellement par les relais inguinaux profonds (2), la plupart des troncs aboutissent à des relais rétro-cruraux (3). Il existe ici trois voies principales iliaques externes. Un seul relais ganglionnaire y est perceptible (4). Un petit ganglion iliaque primitif (5) est présent.

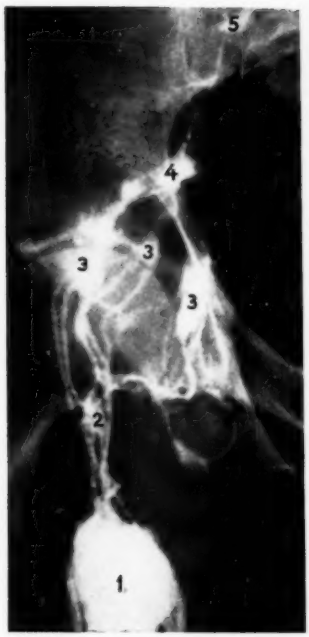

Fig. 5. Un gros ganglion inflammatoire inguinal superficiel est opacifié de façon diffuse (1). Le reste du lymphadénogramme est normal: il existe un ganglion profond (2), trois voies rétro-crurales et leurs relais ganglionnaires (3), deux relais iliaques externes (4), un ganglion iliaque primitif (5).

Lymphadenogramme normal

L'opacification périphérique porte sur tout le système tronculaire provenant de la division dichotomique du vaisseau intubé. Les lymphatiques suivent le trajet de la veine saphène interne et gardent un calibre pratiquement constant (Fig. 2).

Il existe en général 8 à 12 troncs à l'origine des relais ganglionnaires inguinaux superficiels, mais il est fréquent de constater que le tronc afférent se divise »en pinceau» au moment d'aborder le sinus ganglionnaire.

La réplétion du ganglion se fait du sinus périphérique vers le hile: le ganglion normal se présente sous trois aspects (Fig. 3).

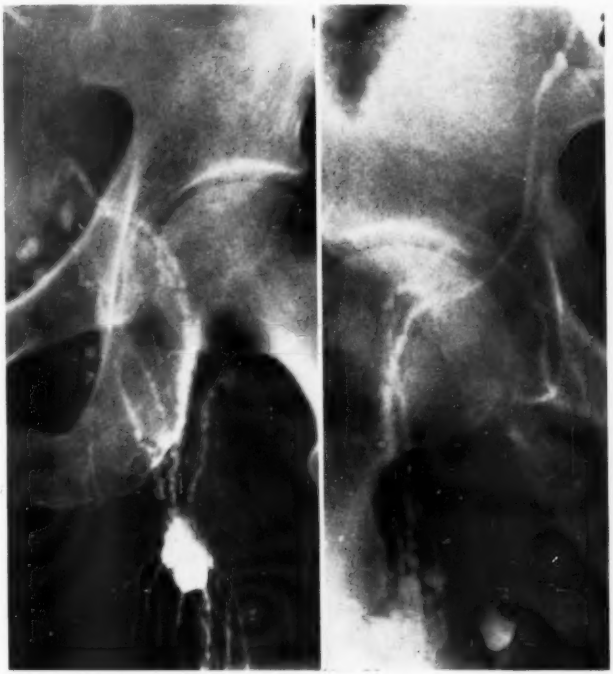

Fig. 6 Fig. 7

Fig. 6. Les voies lymphatiques sont interrompues dès le début de leur trajet pelvien. Dilatation moniliforme des troncs afférents. Aucune voie ne reste entièrement perméable (vérification opératoire).

Fig. 7. Dès les relais inguinaux le produit de contraste ne passe plus par la voie interne (rétro-crurale-iliaque externe, groupe interne) (1). La totalité du produit de contraste est dérivée par la voie externe dilatée.

Le nombre des ganglions inguinaux injectés est variable. Des hiles ganglionnaires, émergent un ou plusieurs efférents de calibre un peu plus large. On distingue deux ou trois voies aboutissant respectivement aux ganglions rétrocruraux externes, internes et moyens. Ces voies peuvent passer par le relais des ganglions inguinaux profonds.

Les efférents des rétrocruraux suivent la voie iliaque externe (groupe externe et groupe interne) où des relais ganglionnaires inconstants, souvent au nombre de deux, peuvent être différenciés.

La voie iliaque externe se continue dans la voie iliaque primitive après un relais inconstant par un ganglion iliaque primitif. L'opacification plus en aval est occasionnelle (Fig. 4).

Fig. 8. Stase lymphatique chronique (associée à stase veineuse). Extrême finesse des troncs lymphatiques périphériques dont le nombre est cependant normal. Il existe dans ce cas un betonnage pelvien et de gros inguinaux sont palpables.

Lymphadenogramme pathologique

Les hyperplasies ganglionnaires non cancéreuses, telles les adénopathies inflammatoires banales, se traduisent par une image élargie, mais dont les caractères structuraux restent conformes à ceux d'un ganglion normal (Fig. 5). En particulier, la réplétion s'effectue du sinus vers le hile de façon homogène en donnant les aspects déjà signalés plus haut.

Caractères radiologiques de l'extension lympho-ganglionnaire ilio-pelvienne des cancers du petit bassin. Notre expérience porte actuellement sur 39 lymphadénographies pelviennes correspondant à des étiologies cancéreuses diverses. On peut observer un arrêt brutal de l'opacification des voies lymphatiques (Fig. 6). Celui-ci peut se présenter au niveau des troncs ou à hauteur d'un ganglion. Dans le premier cas, il s'agit le plus souvent d'une infiltration néoplasique diffuse réalisant un »bétonnage» du bassin. Dans le second cas, il s'agit d'un envahissement ganglionnaire avancé.

Toujours associé à un arrêt (Fig. 7) peut exister un détournement du produit de contraste par des voies demeurées perméables parfois inhabituelles. La sériographie en apporte la meilleure démonstration. A deux reprises, nous avons observé un reflux dans la chaîne hétérolatérale par l'intermédiaire de troncs superficiels du périnée et de troncs pelviens profonds.

Dans le cas d'un blocage partiel ou total, on peut voir une dilatation qui n'intéresse que les afférents directs. Nous n'avons jamais observé de dilatation tronculaire à distance de l'obstacle (Figs. 6 et 7). Il s'agit vraisemblablement d'une image relativement précoce: tardivement, en effet, se produit une atrophie de la voie lymphatique se manifestant par une exiguité anormale et une fragilité excessive des troncs; ils se rompent souvent lors de la réplétion (Fig. 8). L'intubation est d'ailleurs dans ces cas toujours très difficile.

Fig. 9 Fig. 10 Fig. 11

Fig. 9. Un gros ganglion ovalaire iliaque externe est irrégulièrement mis en évidence.

Fig. 10. Une grosse adénopathie iliaque externe est irrégulièrement mise en évidence. Un magma centro-ganglionnaire est séparé du sinus par de larges plages lacunaires. En amont, les troncs sont légèrement dilatés. Stop au-delà de l'adenopathie (vérification opératoire).

Fig. 11. Un ganglion allongé mais dont la réplétion présente des critères normaux est reporté au niveau des limites osseuses (I). A hauteur de la confluence des troncs iliaques internes, le trajet présente une concavité dirigée en-dedans.

Dans certains cas, on observe un défect de la réplétion ganglionnaire: Le schéma d'opacification est bouleversé, il existe des lacunes anarchiques. Cet aspect ne doit pas être confondu avec une réplétion partielle du ganglion (Fig. 9). C'est ainsi qu'une image polaire, se présentant sous forme d'une calotte opaque, est très fréquente à l'état normal.

Un aspect particulier de la réplétion des ganglions néoplasiques consiste en une opacification centro-ganglionnaire primaire irrégulière, alors qu'un ganglion normal montre tout d'abord un liseré sinusal périphérique d'ou s'échappent des rayons opaques à direction hilaire (Fig. 10).

Les troncs lymphatiques peuvent épouser le contour de masses avoisinantes. Les ganglions peuvent également être refoulés hors de leur zone de projection normale (Fig. 11).

Tableau I

Envahissements de la chaîne ganglionnaire inguino-ilio-pelvienne

Nombre d'examens	Signes cliniques			Signes lymphographiques		
	+	-?	—	+	?	—
17	17			(17)		
22		13		(5) 8 3	2	(3)
			9	(7)	2	

(○) diagnostic controlé
\+ signes positifs
-? absence de signes cliniques positifs possibilité-probabilité à ± longue échéance
— signes négatifs

Tableau II

Envahissements de la chaîne ganglionnaire inguino-ilio-pelvienne

Cancer du col de l'utérus		Signes lymphographiques			Contrôle du diagnostic lymphographique		
	Nombre de cas	+	?	—	Intervention histologique	Évolution signes cliniques	Non contrôlés
STADE I	7	5	2		2	3	2
STADE II	2	2					2
STADE III	7	6		1	1	3	3
STADE IV	7	7			5	2	

Resultats

Sur 39 lymphadénographies réalisées dans des cancers du petit bassin, 17 correspondent à des stades avancés ou le diagnostic clinique d'envahissement ganglionnaire est patent. Dans 13 cas, le diagnostic clinique d'envahissement n'est pas fait mais l'atteinte de la voie lymphatique est à redouter à plus ou moins longue échéance. Dans les 9 autres cas, elle ne peut être normalement soupçonnée (Tableau I).

Une étude plus détaillée porte, d'une part, sur les cancers du col de l'utérus, d'autre part, sur les autres tumeurs pelviennes.

Cancer du col de l'utérus

Les résultats de 23 lymphadénographies reprises dans le Tableau II font apparaître les faits suivants.

Table III

Envahissements de la chaîne ganglionnaire inguino-ilio-pelvienne

	Signes cliniques positifs	Signes lymphographiques			Contrôle du diagnostic lymphograpique		
		+	?	—	Intervention histologique	Évolution signes cliniques	Non contrôlés
Cancers de l'ovaire 5 cas	5	5			5		
Maladie de Hodgkin 4 cas	1	3	1		1	2	1
Cancers du rectum 4 cas	3	3	1		3		1
Cancers de vessie 2 cas				2	2		
Cancers de prostate 1 cas	1	1					

Dans les cas avancés, la technique lymph raphique vient confirmer de façon constante les signes cliniques.

Dans les cas douteux, elle apporte soit la certitude d'un envahissement ganglionnaire, soit la présomption d'une absence d'envahissement.

Dans 9 cas où l'on ne peut en aucune façon cliniquement soupçonner une propagation lymphatique, la lymphadenographie montre sept images d'envahissements dont 5 furent contrôlées au cours d'interventions ultérieures.

Tumeurs d'autre origine

Le Tableau III donne les résultats de 16 lymphadénographies effectuées dans des tumeurs d'origines diverses.

Dans tous les cas, la lymphographie confirme et précise le diagnostic clinique d'envahissement.

Dans 3 cas de maladie de Hodgkin, ou n'existe aucune preuve clinique d'adénopathie pelvienne, la lymphadénographie en démontre formellement l'existence.

Dans deux cas de cancer de la vessie, la chaîne est normale. Le fait est confirmé par examen histologique après lymphadénectomie.

Conclusions

La comparaison des résultats obtenus démontre que la méthode lymphadénographique permet:

1. de confirmer l'existence d'envahissements ganglionnaires et d'en préciser l'extension;
2. d'affirmer ou d'infirmer une atteinte macroscopique de la voie lymphatique dans les cas de doute clinique;
3. de mettre en évidence formellement des adénopathies précoces cliniquement insoupçonnables.

Dans notre expérience actuelle, les résultats les plus spectaculaires sont obtenus dans les épithéliomas du col de l'utérus.

RÉSUMÉ

La mise en évidence radiologique de la chaîne ganglionnaire inguino-ilio-pelvienne chez l'homme peut être obtenue par l'injection intra-canaliculaire d'un tronc lymphatique périphérique du membre inférieur, au moyen d'un produit de contraste tri-iodé hydrosoluble. Les caractères du lymphadénogramme normal et d'envahissement néoplasique sont analysés.

SUMMARY

The inguino-ilio-pelvic ganglionic chain in man has been demonstrated by the injection of a tri-iodized water-soluble contrast medium through a cannula into a peripheral lymphatic trunk in a lower limb. The appearances of the normal lymphadenogram as well as those seen in cases of neoplastic invasion are described.

ZUSAMMENFASSUNG

Die Reihe der inguinalen und iliopelvinen Lymphdrüsen beim Menschen sind mit Hilfe einer intrakanalikulären Injektion eines trijodierten wasserlöslichen Kontrastmittels in einen peripheren Lymphstamm der unteren Extremität demonstriert worden. Das Aussehen des normalen Lymphadenogrammes sowie das Aussehen in Fällen mit neoplasmatischer Invasion werden beschrieben.

BIBLIOGRAPHIE

Carvalho, R., Rodriguez, A. et Pereira, S.: Sur la méthode radiographique de mise en évidence des lymphatiques chez le vivant. J. Radiol. d'Électrol. 18 (1934), 180.

Celis, A., Kuthy Porter, J.: Lymphatics of the thorax. An anatomic and radiologic study. Acta radiol. 38 (1952), 461.

COLLETTE, J.-M.: Essais de lymphographie expérimentale. Activité de la Hyaluronidase. J. belge Radiol. 36 (1953), 276.
— Étude radiologique de la circulation plasmo-tissulaire par injection sous-cutanée de substance de contraste. Rev. méd. Liège 8 (1953), 776.
— La microradiographie. Bases et principes de la technique. Une nouvelle application. La microlymphographie. J. belge Radiol. 36 (1953), 293.
— Lymphographie expérimentale et clinique. Description d'une technique d'opacification radiologique du système lymphatique périphérique et du groupe ganglionnaire ilio-pelvien. Acta chir. belg. 6 (1955), 607.
— et TOUSSAINT, R.: Lymphographie expérimentale après lymphadénectomie. Zbl. Radiologica 49 (1956), 33.
DOTTI, E.: Sulla circulazione linfatica in condizioni pathologiche. Ann. radiol. Fis. med. 9 (1935), 190.
KINMONTH, J. B.: Lymphangiography by radiological methods. J. Fac. Radiol. 6 (1955), 217.
SERVELLE, M.: A propos de la lymphographie expérimentale et clinique. J. radiol. Électrol. 26 (1944/45), 165.
TENEFF, S. et STOPPANI, F.: A propos de la lymphographie. J. radiol. Électrol. 20 (1936), 74.
VARADY, B.: Radiographie du système lymphatique de l'utérus. Schweiz. Med. Wschr. 18 (1947), 509.
WEYENETH, R.: L'hépato-splénographie au moyen de l'hépatosélectan (sol iodé) avec élimination rapide de la substance de contraste. Schweiz. Med. Wschr. 1 (1944), 16.

BOOK REVIEWS

EXPERIMENTAL STUDIES ON THE DISAPPEARANCE OF RADIOSODIUM IONS FROM LOCAL DEPOSITS IN THE CAVITY AND IN THE WALL OF THE VAGINA OF THE RAT. By Björn Westin. 87 pages, 42 illustrations. Acta radiol. Suppl. 144 (1957). Sw. Kr. 30: —.

The so-called absorptive capacity of the vagina has been a subject for investigation in human beings as well as in animals. A large number of substances have been reported as being absorbed by the vagina; possible absorption through the uterine cervix has, however, not been excluded and the substances have often been used in unphysiologic concentrations, probably causing local damage to the vaginal mucosa. Only a few investigators have paid attention to the possible changes in the absorptive capacity of the vagina caused by fluctuations in the hormonal condition of the experimental subject. Such alterations in the absorptive capacity of the vagina may be dependent partly on changes in the vaginal membrane and partly on changes in the regional circulation.

In the present paper, both these changes were studied by means of the disappearance technique used by KETY. The applicability of Kety's formula to intracavital disappearance measurements was proved experimentally; it is stressed that the disappearance constant has another meaning in intracavital measurements.

Local damage to the vagina was avoided by the use of a physiologic substance (sodium chloride) in a physiologic concentration. For various reasons the most convenient isotope for the experiments was radiosodium (Na^{22}). The investigations were performed on the rat, because the vaginal epithelium of this animal reacts favourably to oestrogen, permitting the study of the penetration of a substance through a membrane varying in thickness and structure. An accurate experimental method which permits careful numerical evaluation of the disappearance constant has been worked out. The injections of the radioisotope were performed with great accuracy and the volume injected was kept constant. Corrections were made for physical, residual, and actual animal background. Errors in the evaluation of the disappearance constant were studied and found to be small.

It has been shown in experiments on hystero-ovariectomized rats, that the vagina has a true absorptive capacity and its magnitude is given in $\%\ min^{-1}\ cm^{-2}$. The intracavital radiosodium disappearance was significantly higher in untreated animals than in animals having a cornified vaginal membrane; the intramural radiosodium disappearance was not significantly increased following oestrogenic treatment. The existence of a barrier to sodium ions between the intracavital and the intramural deposits is pointed out. Its function was found to be partly dependent on local changes in the vaginal membrane induced by oestradiol-mono-benzoate.

In similar experiments in ovariectomized rats it was shown that the intracavital radiosodium disappearance for untreated and oestrogen-treated animals was of the same magnitude as in hystero-ovariectomized rats. The intramural radiosodium disappearance in ovariectomized animals was slightly lower than in hystero-ovariectomized animals. It was concluded that an appreciable disappearance via the cervix would have resulted in a higher intracavital disappearance constant than that observed experimentally.

A few experiments on the mechanism of the disappearance from the vaginal wall and cavity were performed. Some of these involving the possible role of lymph flow in intramural disappearance measurements suggested that the latter was mainly governed by the endocapillary blood-flow. Histologic investigations indicated that a slight degree of local inflammation in the vaginal wall might be present in untreated animals subjected to repeated intramural disappearance measurements.

In the intracavital group a few experiments were performed in order to reduce the barrier of the oestric vaginal membrane. Certain enzymes such as phospholipase, trypsin and hyaluronidase, when applied to the vagina, were incapable of changing the intracavital radiosodium disappearance. Experiments on colchicine indicated that the radiosodium disappearance was inhibited when the oestric vaginal mucosa was cornified but increased when the cornification was partly inhibited. The experiments seemed to indicate that the oestric vaginal barrier was produced by substances other than those split up by the enzymes used, and, furthermore, that the oestric vaginal barrier was localized to the superficial layers of the vaginal mucosa. The failure to reduce the barrier of the cornified vaginal membrane should be judged in the light of similar experiments on the skin.

There are theoretically two possible methods of absorption in the skin, transepidermal and transfollicular. It has not been possible to determine with any certainty the absorption by the former route. In this connection it is interesting to note that the radiosodium disappearance from intracavital deposits per unit vaginal area through the glandless cornified vaginal membrane was of the magnitude of 0.07 % min^{-1} cm^{-2}.

Intracavital radiosodium disappearance offers several advantages as a method of investigation. Quantitative measurements may be performed with accuracy. The method can be applied to any cavity or membrane and permits the study of physiologic processes with a minimum of trauma. It reflects true biologic phenomena related to the membrane of the cavity and its regional circulation.

Autoreview.

SELEKTIVE LUNGENANGIOGRAPHIE IN DER PRAEOPERATIVEN DIAGNOSTIK UND IN DER INNEREN KLINIK. Von Wilhelm Bolt, Werner Forssman und Hans Rink. 199 S., 205 Abb. Georg Thieme Verlag, Stuttgart 1957. D.M. 54: —.

The writers of this monograph introduce the term *selective pulmonary angiography*. By this they mean 'investigation of regional morphologic and functional changes in the pulmonary vessels by means of injection of contrast medium through a catheter into previously determined pulmonary vascular areas'. Injections of contrast medium selectively into the cavities of the heart or within the vascular areas of the lungs have usually been designated in the Nordic countries by the frequently somewhat undifferentiated common term of selective angiocardiography (JÖNSSON). Whether or not the term 'selective pulmonary angiography' is justified for the contrast investigations described of peripheral pulmonary vessels is open to discussion. To the majority engaged in catheterization of the pulmonary vessels, the location of the cardiac catheter in a previously determined segmental arterial branch probably seems a difficult accomplishment. If this phase of the investigation cannot in the great majority of cases be mastered, the designation 'selective' is not justified. Unfortunately, the writers do not give any information, other than that already well known, as to how the element of chance in the location of the catheter in a predetermined pulmonary artery may be overcome.

The writers state in the introduction that they consider the value of the method to lie less in its exposure of morphologic changes than in the opportunity it affords for a study of function. In the 'functional analyses of the periphery of the lung' it is stated

that the lumen of the pulmonary vessel is 'usually almost completely' filled by the catheter. This leaves one with an uncomfortable feeling of uncertainty concerning what the essential conditions actually are in these function studies. In those cases where the lumen of the vessel is largely occluded, extremely cautious injection of the contrast medium is recommended in order to avoid rupture of the vessel. In the reviewer's opinion, this is a correct and exceedingly important observation. The functional analysis is performed by observation of the time required for passage of the contrast medium to the pulmonary veins, when a homogeneous, transient 'contrast shadow' is obtained during the capillary phase. This 'shadow' is said to disappear normally within fractions of a second showing that neither capillary nor alveolar regions are damaged either functionally or organically.

A few marginal comments seem to be called for here: The assumption that the contrast medium flows undiluted through the pulmonary capillaries when the catheter about fills the lumen of the vessel is incorrect. Even when there is complete occlusion of the lumen of the vessel by the catheter, there is circulation in the lung distal to the catheter. For one thing, the subsegmental arteries are frequently not terminal arteries and, for another, blood is easily shunted by the bronchial arteries to areas within the lung distal to an occluded pulmonary artery branch. Moreover, it is probable that respiratory displacement of the blood and contrast medium can take place distal to the catheter. The degree of arterialization of the blood distal to a totally or partially occluded pulmonary artery also affects the tonus of the peripheral pulmonary arterial branches and thereby the passage time of the contrast medium. With an unspecified rate of injection and volume of contrast medium in relation to the magnitude of the vascular region, considerable variations in the disappearance of 'the contrast shadow — capillary phase' may be obtained. In addition, the differences in the physical characteristics of contrast medium and blood are of decisive significance in the distribution distal to a totally or partially occluded pulmonary artery. For such reasons it is doubtful if the writers' frequently far-reaching conclusions concerning function based upon selective pulmonary angiography are justified. A constriction of the vessels with retardation of the passage of the contrast medium can scarcely be set up as indications, as done by the writers, of alveolar hypoventilation. The premise that by selective pulmonary angiography it should be possible to differentiate between reversible and irreversible atelectasis, should also be reconsidered.

The writers have studied no less than 2,000 cases angiographically and illustrate numerous interesting pathologic conditions of the lungs. References to the literature take up almost 15 pages. The presentation of the book is excellent, as always by the George Thieme publishing house.

Björn Nordenström.